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(54) Title: SUBTILISIN 309 VARIANTS HAVING DECREASED ADSORPTION AND INCREASED HYDROLYSIS (57) Abstract <p>The present invention relates to subtilisin (309) variants having a modified amino acid sequence of wild-type subtilisin (309) amino acid sequence, the wild-type amino acid sequence comprising a first loop region, a second loop region, a third loop region, a fourth loop region, a fifth loop region and a sixth loop region; wherein the modified amino acid sequence comprises different amino acids than that occurring in wild-type subtilisin (309) (i.e., substitution) at specifically identified positions in one or more of the loop regions whereby the subtilisin (309) variant has decreased adsorption to, and increased hydrolysis of, an insoluble substrate as compared to the wild type subtilisin (309). The present invention also relates to DNA sequence encoding such subtilisin (309) variants. The present invention also relates to compositions comprising such subtilisin (309) variants for cleaning a variety of surfaces.</p>		

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SUBTILISIN 309 VARIANTS HAVING DECREASED ADSORPTION AND INCREASED HYDROLYSIS

TECHNICAL FIELD

5 The present invention relates to novel enzyme variants useful in a variety of cleaning compositions, and the genes encoding such enzyme variants.

BACKGROUND

Enzymes make up the largest class of naturally occurring proteins.
10 Each class of enzyme generally catalyzes (accelerates a reaction without being consumed) a different kind of chemical reaction. One class of enzymes known as proteases, are known for their ability to hydrolyze (break down a compound into two or more simpler compounds with the uptake of the H and OH parts of a water molecule on either side of the chemical bond cleaved)
15 other proteins. This ability to hydrolyze proteins has been taken advantage of by incorporating naturally occurring and protein engineered proteases as an additive to laundry detergent preparations. Many stains on clothes are proteinaceous and wide-specificity proteases can substantially improve removal of such stains.

20 Unfortunately, the efficacy level of these proteins in their natural, bacterial environment, frequently does not translate into the relatively unnatural wash environment. Specifically, protease characteristics such as thermal stability, pH stability, oxidative stability and substrate specificity are not necessarily optimized for utilization outside the natural environment of the
25 enzyme.

 The amino acid sequence of the protease determines the characteristics of the protease. A change of the amino acid sequence of the protease may alter the properties of the enzyme to varying degrees, or may even inactivate the enzyme, depending upon the location, nature and/or
30 magnitude of the change in the amino acid sequence. Several approaches have been taken to alter the wild-type amino acid sequence of proteases in an attempt to improve their properties, with the goal of increasing the efficacy of the protease in the wash environment. These approaches include altering the amino acid sequence to enhance thermal stability and to improve oxidation
35 stability under quite diverse conditions.

 Despite the variety of approaches described in the art, there is a continuing need for new effective variants of proteases useful for cleaning a variety of surfaces.

Objects of the Present Invention

It is an object of the present invention to provide subtilisin 309 enzyme variants having improved hydrolysis versus the wild-type of the enzyme.

It is also an object of the present invention to provide cleaning compositions comprising these subtilisin 309 enzyme variants.

SUMMARY

The present invention relates to subtilisin 309 variants having a modified amino acid sequence of wild-type subtilisin 309 amino acid sequence, the wild-type amino acid sequence comprising a first loop region, a second loop region, a third loop region, a fourth loop region, a fifth loop region and a sixth loop region; wherein the modified amino acid sequence comprises different amino acids than that occurring in wild-type subtilisin 309 (i.e., substitution) at specifically identified positions in one or more of the loop regions whereby the subtilisin 309 variant has decreased adsorption to, and increased hydrolysis of, an insoluble substrate as compared to the wild-type subtilisin 309. The present invention also relates to DNA sequences encoding such subtilisin 309 variants. The present invention also relates to compositions comprising such subtilisin 309 variants for cleaning a variety of surfaces.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1A and Figure 1B depict the amino acid sequences of subtilisin BPN' and subtilisin 309. The top line represents the amino acid sequence of subtilisin BPN' (SEQ ID NO:2), which is derived from *Bacillus amyloliquefaciens*; the bottom line represents the amino acid sequence of subtilisin 309 (SEQ ID NO:1), which is derived from *Bacillus lentus*. The symbol * in the sequence for subtilisin 309 denotes the absence of specific amino acid residues as compared to subtilisin BPN'.

DESCRIPTION

I. Subtilisin 309 Variants

This invention pertains to subtilisin enzymes, in particular subtilisin 309, that have been modified by mutating the various nucleotide sequences that code for the enzyme, thereby modifying the amino acid sequence of the enzyme. The modified subtilisin enzymes (hereinafter, "subtilisin 309 variants") of the present invention have decreased adsorption to and increased hydrolysis of an insoluble substrate as compared to the wild-type subtilisin. The present invention also pertains to the mutant genes encoding for such subtilisin 309 variants.

When referring to the amino acid sequence of native subtilisin 309

(having 269 amino acid residues), the amino acid sequence of subtilisin BPN' (having 275 amino acid residues) is frequently used as the standard. The use of "BPN' numbering" has become the conventional method for identifying residue positions in all subtilisins. The amino acid sequences for native subtilisin BPN' and native subtilisin 309 are set forth in Figs 1A and 1B. The symbol "*" in the sequence for subtilisin 309 in Figs 1A and 1B denotes the absence of specific amino acid residues compared to native subtilisin BPN'. However, for purposes of discussion herein, reference to amino acid positions shall be based on "true" subtilisin 309 numbering (e.g., refer to SEQ ID NO:1, discussed below).

The subtilisin 309 enzymes of this invention belong to a class of enzymes known as proteases. A protease is a catalyst for the cleavage of peptide bonds. One type of protease is a serine protease. A serine protease is distinguished by the fact that there is an essential serine residue at the active site.

The observation that an enzyme's rate of hydrolysis of soluble substrates increases with enzyme concentration is well documented. It would therefore seem plausible that for surface bound substrates, such as is encountered in many cleaning applications, the rate of hydrolysis would increase with increasing surface concentration. This has been shown to be the case. (Brode, P.F. III and D. S. Rauch, *LANGMUIR*, "Subtilisin BPN': Activity on an Immobilized Substrate", Vol. 8, pp. 1325-1329 (1992)). In fact, a linear dependence of rate upon surface concentration was found for insoluble substrates when the surface concentration of the enzyme was varied. (Rubingh, D. N. and M. D. Bauer, "Catalysis of Hydrolysis by Proteases at the Protein-Solution Interface," in *POLYMER SOLUTIONS, BLENDS AND INTERFACES*, Ed. by I. Noda and D. N. Rubingh, Elsevier, p. 464 (1992)). Surprisingly, when seeking to apply this principle in the search for variant proteases which give better cleaning performance, we did not find that enzymes which adsorb more give better performance. In fact, we surprisingly determined the opposite to be the case: decreased adsorption by an enzyme to a substrate resulted in increased hydrolysis of the substrate (i.e., better cleaning performance).

While not wishing to be bound by theory, it is believed that improved performance, when comparing one variant to another, is a result of the fact that enzymes which adsorb less are also less tightly bound and therefore more highly mobile on the surface from which the insoluble protein substrate is to be removed. At comparable enzyme solution concentrations, this increased mobility is sufficient to outweigh any advantage that is conferred by delivering

a higher concentration of enzyme to the surface.

The mutations described herein are designed to change (i.e., decrease) the adsorption of the enzyme to surface-bound soils. In subtilisin 309, certain amino acids form exterior loops on the enzyme molecule. For purposes of discussion, these loops shall be referred to as the first, second, third, fourth and fifth loop regions. Specifically, positions 57-64 form the first loop region; positions 93-105 form the second loop region; positions 124-131 form the third loop region; positions 152-161 form the fourth loop region; positions 181-185 form the fifth loop region; and positions 193-214 form the sixth loop region (position numbering analagous to positions in the amino acid sequence for wild-type subtilisin 309 (SEQ ID NO:1)).

It is believed that these loop regions play a significant role in the adsorption of the enzyme molecule to a surface-bound peptide, and specific mutations in one or more of these loop regions will have a significant effect on this adsorption. While not wishing to be bound by theory, it is believed that the loop regions are important to the adsorption of the subtilisin 309 molecule for at least two reasons. First, the amino acids which comprise the loop regions can make close contacts with any surfaces to which the molecule is exposed. Second, the proximity of the loop regions to the active-site and binding pocket of the subtilisin 309 molecule gives them a role in the catalytically productive adsorption of the enzyme to surface-bound substrates (peptides/protein soils).

The following is a list of abbreviations used herein to describe amino acids:

	Amino Acid	Three-letter Abbreviation	One-letter Symbol
	Alanine	Ala	A
	Arginine	Arg	R
	Asparagine	Asn	N
5	Aspartic Acid	Asp	D
	Asparagine or Aspartic Acid	Asp	D
	Cysteine	Cys	C
	Glutamine	Gln	Q
	Glutamic Acid	Glu	E
10	Glutamine or Glutamic Acid	Glx	Z
	Glycine	Gly	G
	Histidine	His	H
	Isoleucine	Ile	I
	Leucine	Leu	L
15	Lysine	Lys	K
	Methionine	Met	M
	Phenylalanine	Phe	F
	Proline	Phe	F
	Serine	Ser	S
20	Threonine	Thr	T
	Tryptophan	Trp	W
	Tyrosine	Tyr	Y
	Valine	Val	V
	No amino acid at position	Xaa	*

25 As used herein, "variant" means an enzyme having an amino acid sequence which differs from that of wild-type.

As used herein, "mutant subtilisin 309 DNA sequence" means a DNA sequence coding for a subtilisin 309 variant.

30 As used herein, "wild-type subtilisin 309" refers to an enzyme represented by SEQ ID NO:1. The amino acid sequence for subtilisin 309 is further described in World Patent Publication 89/06279 (1989), incorporated herein by reference. See also, World Patent Publication 94/02618, published February 3, 1994 by Mulleners et al.

35 As used herein, the term "subtilisin 309 wild-type amino acid sequence" encompasses SEQ ID NO:1 as well as SEQ ID NO:1 having modifications to the amino acid sequence other than at any of positions 57-64, 93-105, 124-131, 152-161, 181-185 and 193-214.

As used herein, "more hydrophilic amino acid" refers to any other amino

acid having greater hydrophilicity than a subject amino acid with reference to the hydrophilicity table below. The following hydrophilicity table (Table 1) lists amino acids in descending order of increasing hydrophilicity (see Hopp, T.P., and Woods, K.R., "Prediction of Protein Antigenic Determinants from Amino Acid Sequences", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCE USA, Vol. 78, pp. 3824-3828, 1981, incorporated herein by reference).

TABLE 1

	Amino Acid	Hydrophilicity Value
	Trp	-3.4
10	Phe	-2.5
	Tyr	-2.3
	Leu, Ile	-1.8
	Val	-1.5
	Met	-1.3
15	Cys	-1.0
	Ala, His	-0.5
	Thr	-0.4
	Pro, Gly	-0.0
	Gln, Asn	0.2
20	Ser	0.3
	Arg ⁺ , Lys ⁺ , Glu ⁻ , Asp ⁻	3.0

Table 1 also indicates which amino acids carry a charge (this characteristic being based on a pH of from about 8-9). The positively charged amino acids are Arg and Lys, the negatively charged amino acids are Glu and Asp, and the remaining amino acids are neutral. In a preferred embodiment of the present invention, the substituting amino acid is either neutral or negatively charged, more preferably negatively charged (i.e., Glu or Asp).

Therefore, for example, the statement "substitute Gln with an equally or more hydrophilic amino acid which is neutral or has a negative charge" means Gln would be substituted with Asn (which is equally hydrophilic to Gln), or Ser, Glu or Asp (which are more hydrophilic than Gln); each of which are neutral or have a negative charge, and have a greater hydrophilicity value as compared to Gln. Likewise, the statement "substitute Pro with a more hydrophilic amino acid which is neutral or has a negative charge" means Pro would be substituted with Gln, Asn, Ser, Glu or Asp.

A. Loop Region 6 Substitution Variants

1. Variants comprising at least one amino acid substitution

In one embodiment of the present invention, the subtilisin 309 variant has a modified amino acid sequence of subtilisin 309 wild-type amino acid sequence, wherein the modified amino acid sequence comprises a substitution at one or more of positions 193, 194, 195, 196, 197, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213 or 214; whereby the subtilisin 309 variant has decreased adsorption to, and increased hydrolysis of, an insoluble substrate as compared to the wild-type subtilisin 309. Preferably, the positions having a substituted amino acid are 193, 194, 195, 196, 199, 201, 202, 203, 204, 205, 206 or 209; more preferably, 194, 195, 196, 199 or 201.

Preferably, the substituting amino acid for position 193 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Pro, Ser or Thr.

Preferably, the substituting amino acid for position 194 is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

Preferably, the substituting amino acid for position 195 is Asn, Asp, Gln, Glu, Gly, Ser.

Preferably, the substituting amino acid for position 196 is Asn, Asp, Gln, Glu, Pro or Ser.

Preferably, the substituting amino acid for position 197 is Ala, Asp, Cys, Gln, Glu, Gly, His, Met, Pro or Ser.

Preferably, the substituting amino acid for position 199 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

Preferably, the substituting amino acid for position 200 is Asn, Asp, Glu or Ser.

Preferably, the substituting amino acid for position 201 is Asp or Glu.

Preferably, the substituting amino acid for position 202 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

Preferably, the substituting amino acid for position 203 is Ala, Asn, Asp, Gln, His, Ile, Met, Pro or Ser.

Preferably, the substituting amino acid for position 204 is Asn, Asp, Gln, Glu, Gly or Ser.

Preferably, the substituting amino acid for position 205 is Asn, Asp, Gln, Glu, Pro or Ser.

Preferably, the substituting amino acid for position 206 is Asp or Glu.

Preferably, the substituting amino acid for position 207 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

Preferably, the substituting amino acid for position 208 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Pro or Val.

Preferably, the substituting amino acid for position 209 is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

5 Preferably, the substituting amino acid for position 210 is Asp or Glu.

Preferably, the substituting amino acid for position 211 is Ala, Asn, Asp, Cys, Gln, Gly, His, Ile, Met, Pro, Ser, Thr or Val.

Preferably, the substituting amino acid for position 212 is Glu.

10 Preferably, the substituting amino acid for position 213 is Asn, Asp, Gln, Glu, Pro or Ser.

Preferably, the substituting amino acid for position 214 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

15 More preferably, the substituting amino acid for any of positions 193, 194, 195, 196, 197, 199, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213 and 214 is, with reference to Table 1, is neutral or negatively charged and equally or more hydrophilic, preferably more hydrophilic, than the amino acid at the subject position in wild-type subtilisin 309.

20 More preferably still, the substituting amino acid for any of positions 193, 194, 195, 196, 197, 199, 200, 201, 202, 204, 205, 206, 207, 208, 209, 210, 212, 213 and 214 is Asp or Glu; and the substituting amino acid for positions 203 and 211 is Asp.

2. Variants comprising at least two amino acid substitutions

25 In another embodiment of the present invention, the subtilisin 309 variant has a modified amino acid sequence of subtilisin 309 wild-type amino acid sequence, wherein the modified amino acid sequence comprises a substitution at two or more of positions 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213 or 214; whereby the subtilisin 309 variant has decreased adsorption to, and increased hydrolysis of, an insoluble substrate as compared to wild-type subtilisin 309.

30 Preferably, the positions having a substituting amino acid are 193, 194, 195, 199, 201, 202, 203, 204, 205, 206, or 209; more preferably, positions 194, 195, 196, 211 or 213.

Preferably, the substituting amino acid for position 193 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser and Thr.

35 Preferably, the substituting amino acid for position 194 is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

Preferably, the substituting amino acid for position 195 is Asn, Asp, Gln, Glu, Gly or Ser.

Preferably, the substituting amino acid for position 196 is Asn, Asp, Gln, Glu, Pro or Ser.

Preferably, the substituting amino acid for position 197 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

5 Preferably, the substituting amino acid for position 198 is Asp, Gln, Glu or Ser.

Preferably, the substituting amino acid for position 199 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

10 Preferably, the substituting amino acid for position 200 is Asn, Asp, Glu or Ser.

Preferably, the substituting amino acid for position 201 is Asp or Glu.

Preferably, the substituting amino acid for position 202 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

15 Preferably, the substituting amino acid for position 203 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Met, Pro, Ser or Thr.

Preferably, the substituting amino acid for position 204 is Asn, Asp, Gln, Glu, Gly or Ser.

Preferably, the substituting amino acid for position 205 is Asn, Asp, Gln, Glu, Pro or Ser.

20 Preferably, the substituting amino acid for position 206 is Asp or Glu.

Preferably, the substituting amino acid for position 207 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

Preferably, the substituting amino acid for position 208 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Pro or Val.

25 Preferably, the substituting amino acid for position 209 is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

Preferably, the substituting amino acid for position 210 is Asp or Glu.

Preferably, the substituting amino acid for position 211 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Met, Pro, Ser, Thr or Val.

30 Preferably, the substituting amino acid for position 212 is Asp, Gln, Glu or Ser. However, if position 211 is substituted with Asn, Glu or Val, then position 212 is not substituted with Asp.

Preferably, the substituting amino acid for position 213 is Asn, Asp, Gln, Glu, Pro or Ser.

35 Preferably, the substituting amino acid for position 214 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

More preferably, the substituting amino acid for any of positions 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208,

209, 210, 211, 212, 213 or 214 is, with reference to Table 1, is neutral or negatively charged and equally or more more hydrophilic, preferably more hydrophilic, than the amino acid at the subject position in wild-type subtilisin 309.

5 More preferably still, the substituting amino acid for any of positions 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213 or 214 is Asp and Glu.

3. Variants comprising at least three amino acid substitutions

10 In another embodiment of the present invention, the subtilisin 309 variant has a modified amino acid sequence of subtilisin 309 wild-type amino acid sequence, wherein the modified amino acid sequence comprises a substitution at three or more of positions 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213 or 214; whereby the subtilisin 309 variant has decreased adsorption to, and increased
15 hydrolysis of, an insoluble substrate as compared to wild-type subtilisin 309. Preferably, the positions having a substituting amino acid are 193, 194, 195, 199, 201, 202, 203, 204, 205, 206, or 209; more preferably, positions 194, 195, 196, 211 or 213.

20 Preferably, the substituting amino acid for position 193 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

 Preferably, the substituting amino acid for position 194 is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

 Preferably, the substituting amino acid for position 195 is Asn, Asp, Gln, Glu, Gly or Ser.

25 Preferably, the substituting amino acid for position 196 is Asn, Asp, Gln, Glu, Pro or Ser.

 Preferably, the substituting amino acid for position 197 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

30 Preferably, the substituting amino acid for position 198 is Asp, Gln, Glu or Ser.

 Preferably, the substituting amino acid for position 199 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

 Preferably, the substituting amino acid for position 200 Asn, Asp, Glu or Ser.

35 Preferably, the substituting amino acid for position 201 is Asp or Glu.

 Preferably, the substituting amino acid for position 202 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

 Preferably, the substituting amino acid for position 203 is Ala, Asn, Asp,

Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Pro, Ser, Thr or Val.

Preferably, the substituting amino acid for position 204 is Asn, Asp, Gln, Glu, Gly or Ser.

Preferably, the substituting amino acid for position 205 is Asn, Asp, Gln, Glu, Pro or Ser.

Preferably, the substituting amino acid for position 206 is Asp or Glu.

Preferably, the substituting amino acid for position 207 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

Preferably, the substituting amino acid for position 208 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Pro, Thr or Val.

Preferably, the substituting amino acid for position 209 is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

Preferably, the substituting amino acid for position 210 is Asp or Glu.

Preferably, the substituting amino acid for position 211 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Met, Pro, Ser, Thr or Val.

Preferably, the substituting amino acid for position 212 is Asp, Gln, Glu or Ser.

Preferably, the substituting amino acid for position 213 is Asn, Asp, Gln, Glu, Pro or Ser.

Preferably, the substituting amino acid for position 214 is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

More preferably, the substituting amino acid for any of positions 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213 or 214 is, with reference to Table 1, is neutral or negatively charged and equally or more hydrophilic, preferably more hydrophilic, than the amino acid at the subject position in wild-type subtilisin 309.

More preferably still, the substituting amino acid for any of positions 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 208, 209, 210, 211, 212, 213 or 214 is Asp or Glu.

B. Multi-Loop Regions Substitution Variants

In another embodiment of the present invention, the subtilisin 309 variant has a modified amino acid sequence of subtilisin 309 wild-type amino acid sequence, wherein the modified amino acid sequence comprises a substitution at one or more positions in one or more of the first, second, third, fourth, or fifth loop regions; whereby the subtilisin 309 variant has decreased adsorption to, and increased hydrolysis of, an insoluble substrate as compared to the wild-type subtilisin 309.

In another embodiment of the present invention, the subtilisin 309 variant further comprises one or more substitutions to the sixth loop region.

In a preferred embodiment of the present invention, the substituting amino acid for one or more of the positions in one or more of the loop regions is, with reference to Table 1, neutral or negatively charged and equally or more hydrophilic, preferably more hydrophilic, than the amino acid at the subject position in the wild-type amino acid sequence.

1. Substitutions in the First Loop Region

When a substitution occurs in the first loop region, the substitution occurs at one or more of positions 57, 58, 59, 60, 61, 63, or 64.

When a substitution occurs at position 57, the substituting amino acid is Asn, Asp, Glu or Ser.

When a substitution occurs at position 58, the substituting amino acid is Glu.

When a substitution occurs at position 59, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 60, the substituting amino acid is Asp, Gln, Glu or Ser.

When a substitution occurs at position 61, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 63, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 64, the substituting amino acid is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

2. Substitutions in the Second Loop Region

When a substitution occurs in the second loop region, the substitution occurs at one or more of positions 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, or 105.

When a substitution occurs at position 93, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

When a substitution occurs at position 94, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Met, Pro, Ser, Thr or Val.

When a substitution occurs at position 95, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 96, the substituting amino acid is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

When a substitution occurs at position 97, the substituting amino acid is Asp or Glu.

When a substitution occurs at position 98, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 99, the substituting amino acid is Asp or Glu.

5 When a substitution occurs at position 100, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 101, the substituting amino acid is Asp or Glu.

10 When a substitution occurs at position 102, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

When a substitution occurs at position 103, the substituting amino acid is Asp or Glu.

When a substitution occurs at position 104, the substituting amino acid is Asp or Glu.

15 When a substitution occurs at position 105, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Leu, Met, Pro, Ser, Thr or Val.

3. Substitutions in the Third Loop Region

When a substitution occurs in the third loop region, the substitution occurs at one or more of positions 124, 125, 126, 127, 128, 129, 130 or 131.

20 When a substitution occurs at position 124, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Met, Pro, Ser, Thr or Val.

When a substitution occurs at position 125, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

25 When a substitution occurs at position 126, the substituting amino acid is Asp or Glu.

When a substitution occurs at position 127, the substituting amino acid is Asn, Asp, Gln, Glu, Gly or Ser.

When a substitution occurs at position 128, the substituting amino acid is Asp or Glu.

30 When a substitution occurs at position 129, the substituting amino acid is Asn, Asp, Gln, Glu, Gly or Ser.

When a substitution occurs at position 130, the substituting amino acid is Asp or Glu.

35 When a substitution occurs at position 131, the substituting amino acid is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser, Thr.

4. Substitutions in the Fourth Loop Region

When a substitution occurs in the fourth loop region, the substitution occurs at one or more of positions 152, 153, 154, 155, 156, 157, 158, 159, 160

or 161.

When a substitution occurs at position 152, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 153, the substituting amino acid
5 is Asp, Gln, Glu or Ser.

When a substitution occurs at position 154, the substituting amino acid is Asp or Glu.

When a substitution occurs at position 155, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

10 When a substitution occurs at position 156, the substituting amino acid is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

When a substitution occurs at position 157, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 158, the substituting amino acid
15 is Asp or Glu.

When a substitution occurs at position 159, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Leu, Met, Pro, Ser, Thr or Val.

When a substitution occurs at position 160, the substituting amino acid is Asp or Glu.

20 When a substitution occurs at position 161, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Pro, Ser, Thr or Val.

5. Substitutions in the Fifth Loop Region

When a substitution occurs in the fifth loop region, the substitution occurs at one or more of positions 181, 182, 183, 184 or 185.

25 When a substitution occurs at position 181, the substituting amino acid is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

When a substitution occurs at position 182, the substituting amino acid is Asp or Glu.

30 When a substitution occurs at position 183, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Pro, Ser, Thr, Tyr or Val.

When a substitution occurs at position 184, the substituting amino acid is Asp or Glu.

35 When a substitution occurs at position 185, the substituting amino acid is Asn, Asp, Glu or Ser.

6. Substitutions in the Sixth Loop Region

When a substitution occurs in the sixth loop region, in conjunction with one or more substitutions in one or more of the preceding five loop regions,

the substitution occurs at one or more of positions 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213 or 214.

When a substitution occurs at position 193, the substituting amino acid
5 is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

When a substitution occurs at position 194, the substituting amino acid
is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

When a substitution occurs at position 195, the substituting amino acid
is Asn, Asp, Gln, Glu, Gly or Ser.

10 When a substitution occurs at position 196, the substituting amino acid
is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 197, the substituting amino acid
is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

15 When a substitution occurs at position 198, the substituting amino acid
is Asp, Gln, Glu or Ser.

When a substitution occurs at position 199, the substituting amino acid
is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Met, Pro, Ser or Thr.

When a substitution occurs at position 200, the substituting amino acid
is Asn, Asp, Glu or Ser.

20 When a substitution occurs at position 201, the substituting amino acid
is Asp or Glu.

When a substitution occurs at position 202, the substituting amino acid
is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

25 When a substitution occurs at position 203, the substituting amino acid
is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Pro, Ser, Thr or Val.

When a substitution occurs at position 204, the substituting amino acid
is Asn, Asp, Gln, Glu, Gly or Ser.

When a substitution occurs at position 205, the substituting amino acid
is Asn, Asp, Gln, Glu, Pro or Ser.

30 When a substitution occurs at position 206, the substituting amino acid
is Asp or Glu.

When a substitution occurs at position 207, the substituting amino acid
is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

35 When a substitution occurs at position 208, the substituting amino acid
is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Pro, Ser, Thr or Val.

When a substitution occurs at position 209, the substituting amino acid
is Asn, Asp, Gln, Glu, Gly, His, Pro, Ser or Thr.

When a substitution occurs at position 210, the substituting amino acid

is Asp or Glu.

When a substitution occurs at position 211, the substituting amino acid is Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Met, Pro, Ser, Thr or Val.

When a substitution occurs at position 212, the substituting amino acid
5 is Asp, Gln, Glu or Ser.

When a substitution occurs at position 213, the substituting amino acid is Asn, Asp, Gln, Glu, Pro or Ser.

When a substitution occurs at position 214, the substituting amino acid is Asn, Asp, Gln, Glu, Gly, Pro or Ser.

10 C. Additional substitutions at positions other than the loop regions

As indicated hereinbefore, in addition to the one or more substitutions made to the first, second, third, fourth, fifth and/or sixth loop regions of wild-type subtilisin 309, substitutions may be made at positions other than positions in such loop regions (hereafter referred to as "additional substitution"). In
15 another embodiment of the present invention, the subtilisin 309 variant has a modified amino acid sequence of subtilisin 309 wild-type amino acid sequence wherein, in addition to being substituted at one or more positions in one or more of the above-discussed loop regions, there is substitution at position 74. The additional substitution may occur at position 74 alone (preferred), or in
20 combination with one or more additional substitutions.

Where the additional substitution to the subtilisin 309 variant is at position 74 alone, the substitution is preferably with Asn, Asp, Glu, Gly, His, Lys, Phe or Pro. Particularly preferred is where the substitution is with Asp or His.

25 Where there is more than one additional substitution to the subtilisin 309 variant, preferred is where the additional substitutions occur at position 74 in combination with one or more of the following residues: 97, 99, 101, 102, 105 and 121. Preferred additional substitution combinations include the following: 74/97; 74/99; 74/101; 74/102; 74/105; 74/121; 74/97/99; 74/97/101;
30 74/97/102; 74/99/101; 74/99/102; 74/101/102; 74/102/105; 74/102/121; 74/105/121; 74/97/99/101; 74/97/99/102; 74/97/101/102; 74/99/101/102; 74/101/102/121; 74/102/105/121; 74/97/99/101/102; 74/97/101/102/121 and/or 74/97/99/101/102/121. Most preferred additional substitution combinations include the following: 74/97; 74/102; 74/97/102; 74/101/102;
35 74/102/105; 74/99/101/102; 74/97/99/101/102 and 74/99/102.

Preferably, the additional substitutions to be made at each of the identified amino acid residue positions include but are not limited to substitutions at position 74 including Asp, His, Glu, Gly, Phe, Lys, Pro and

Asn; substitutions at position 97 including Asp, Thr, Asn, Gln, Gly and Ser; substitutions at position 99 including Gly, Asp, Lys, Leu, Ala, Glu and Ser; substitutions at position 101 including Gln, Thr, Asp, Glu, Tyr, Lys, Gly, Arg and Ser; substitutions at position 102 including Ser, Tyr, Ile, Leu, M, Ala, W, Asp, Thr, Gly and Val; substitutions at position 105 including Val, Leu, M, Tyr, Gly, Glu, Phe, Thr, Ser, Ala and Ile; and substitutions at position 121 including Asn, Thr, Ile and Ser. The specifically preferred amino acid(s) to be substituted at each such position are designated below in Table 2. Although specific amino acids are shown in Table 2, it should be understood that any amino acid may be substituted at the identified residues. As indicated herein before, these substitutions are in addition to the one or more substitutions at one or more of the loop regions, discussed above.

TABLE 2

	Amino Acid Residue	Preferred Amino Acid to be Substituted/Inserted
15	74	Asp, His
	97	Asp, Thr, Asn, Gly
	99	Arg, Gly, Asp, Lys, Leu, Ala, Glu
	101	Ala, Gln, Thr, Asp, Glu, Tyr, Lys, Gly, Arg
	102	Ile, Tyr, Ser, Leu, Ala, Thr, Gly
20	105	Val, Leu, Tyr, Gly, Phe, Thr, Ser, Ala
	121	Ser, Thr, Ile

D. Preparation of enzyme variants

Example 1

Mutant 309 DNA Sequences

25 A phagemid (pJMA602) containing the wild type subtilisin 309 (i.e., savinase) gene is constructed. The 2.8 Kbp *Pvu* II restriction enzyme fragment of plasmid pUC119, (Vieira, J. and Messing, J., "Production of Single-Stranded Plasmid DNA", 153 METHODS IN ENZYMOLOGY 3-11 (1989)) is cloned into the *Pvu* II site of plasmid pUB110 (Bacillus Genetic Stock Center, Columbus, OH 30 1E9). The pUC119-pUB110 hybrid plasmid is named pJMA601. Into the *Bam*H I restriction site of pJMA601 is cloned the polymerase chain reaction-amplified 309 (savinase) gene from *Bacillus lentus* chromosomal DNA (National Collections of Industrial and Marine Bacteria *Bacillus lentus* 10309) giving phagemid pJMA602. Phagemid pJMA602 is transformed into 35 *Escherichia coli* ung-strain CJ236 and a single stranded uracil-containing DNA template is produced using the VCSM13 helper phage (Kunkel, T.A., J.D. Roberts and R.A. Zakour, "Rapid and efficient site-specific mutagenesis

without phenotypic selection", METHODS IN ENZYMOLOGY, Vol. 154, pp. 367-382, (1987); as modified by Yuckenberg, P.D., F. Witney, J. Geisselsoder and J. McClary, "Site-directed in vitro mutagenesis using uracil-containing DNA and phagemid vectors", DIRECTED MUTAGENESIS - A PRACTICAL APPROACH, ed. M.J. McPherson, pp. 27-48, (1991); both of which are incorporated herein by reference). A single primer site-directed mutagenesis modification of the method of Zoller and Smith (Zoller, M.J., and M. Smith, "Oligonucleotide-directed mutagenesis using M13-derived vectors: an efficient and general procedure for the production of point mutations in any fragment of DNA", NUCLEIC ACIDS RESEARCH, Vol. 10, pp. 6487-6500, (1982), incorporated herein by reference) is used to produce all mutants (basically as presented by Yuckenberg, et al., 1991, above). Oligonucleotides are made using an Applied Biosystem Inc. 380B DNA synthesizer. Mutagenesis reaction products are transformed into Escherichia coli strain MM294 (American Type Culture Collection E. Coli. 33625). All mutants are confirmed by DNA sequencing and the isolated DNA is transformed into the Bacillus subtilis expression strain BG2036 (Yang, M. Y., E. Ferrari and D. J. Henner, (1984), "Cloning of the Neutral Protease Gene of Bacillus subtilis and the Use of the Cloned Gene to Create an In Vitro-derived Deletion Mutation", JOURNAL OF BACTERIOLOGY, Vol. 160, pp. 15-21). For some of the mutants a modified pJMA602 with a frameshift-stop codon mutation in the corresponding loop is used to produce the uracil template. Oligonucleotides are designed to restore the proper reading frame at position 203 and also encoded for random substitutions at positions 57, 58, 59, 60, 61, 63, 64, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 124, 125, 126, 127, 128, 129, 130, 131, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 181, 182, 183, 184, 185, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213 and 214 (equimolar and/or variable mixtures of all four nucleotides for all three bases at these codons). Mutations that correct for the frameshift-stop and produce a functional enzyme are identified by their ability to digest casein. The random substitutions are determined by DNA sequencing.

Example 2

Fermentation

The Bacillus subtilis cells (BG2036) containing a subtilisin mutant of interest are grown to mid-log phase in a one liter culture of LB-glucose broth and inoculated into a Biostat ED fermenter (B. Braun Biotech, Inc., Allentown, Pennsylvania) in a total volume of 10 liters. The fermentation media contains Yeast Extract, starch, antifoam, buffers and trace minerals (see FERMENTATION:

A PRACTICAL APPROACH, Ed. B. McNeil and L. M. Harvey, 1990). The broth is kept at a constant pH of 7.0 during the fermentation run. Chloramphenicol is added for antibiotic selection of mutagenized plasmid. The cells are grown overnight at 37°C to an A_{600} of about 60 and harvested.

Example 3

Purification

The fermentation broth is taken through the following steps to obtain pure enzyme. The broth is cleared of *Bacillus subtilis* cells by centrifugation, and clarified by removing fine particulates with a 100K cutoff membrane. This is followed by concentration on a 10K cutoff membrane, and flow dialysis to reduce the ionic strength and adjust the pH to 5.5 using 0.025M MES buffer (2-(N-morpholino)ethanesulfonic acid). The enzyme is further purified by loading it onto either a cation exchange chromatography column or an affinity adsorption chromatography column and eluting it from the column with a NaCl or a propylene glycol gradient (see Scopes, R. K., PROTEIN PURIFICATION PRINCIPLES AND PRACTICE, Springer-Verlag, New York (1984), incorporated herein by reference).

The pNA assay (DelMar, E.G., C. Largman, J.W. Brodrick and M.C. Geokas, ANAL. BIOCHEM., Vol. 99, pp. 316-320, (1979), incorporated herein by reference) is used to determine the active enzyme concentration for fractions collected during gradient elution. This assay measures the rate at which p-nitroaniline is released as the enzyme hydrolyzes the soluble synthetic substrate, succinyl-alanine-alanine-proline-phenylalanine-p-nitroanilide (sAAPF-pNA). The rate of production of yellow color from the hydrolysis reaction is measured at 410 nm on a spectrophotometer and is proportional to the active enzyme concentration. In addition, absorbance measurements at 280 nm are used to determine the total protein concentration. The active enzyme/total-protein ratio gives the enzyme purity, and is used to identify fractions to be pooled for the stock solution.

To avoid autolysis of the enzyme during storage, an equal weight of propylene glycol is added to the pooled fractions obtained from the chromatography column. Upon completion of the purification procedure the purity of the stock enzyme solution is checked with SDS-PAGE (sodium dodecyl sulfate polyacrylamide gel electrophoresis) and the absolute enzyme concentration is determined via an active site titration method using trypsin inhibitor type II-T; turkey egg white purchased from Sigma Chemical Company (St. Louis, Missouri). The measured conversion factors will show which changes made in the enzyme molecule at the various positions result in the

enzyme variant having increased activity over the wild-type, against the soluble substrate pNA.

In preparation for use, the enzyme stock solution is eluted through a Sephadex-G25 (Pharmacia, Piscataway, New Jersey) size exclusion column to
5 remove the propylene glycol and exchange the buffer. The MES buffer in the enzyme stock solution is exchanged for 0.1 M Tris buffer (Tris(hydroxymethyl-aminomethane) containing 0.01M CaCl_2 and pH adjusted to 8.6 with HCl. All experiments are carried out at pH 8.6 in Tris buffer thermostated at 25°C.

E. Characterization of Enzyme Variants

Example 4

Model Surface Preparation

Aminopropyl controlled pore glass (CPG) purchased from CPG Inc. (Fairfield, New Jersey) is used as a support for covalently attaching the sAAPF-pNA substrate purchased from Bachem, Inc. (Torrence, California).
15 The reaction is carried out in dimethyl sulfoxide and (1-ethyl-3-[3-(dimethylamino)propyl] carbodiimide hydrochloride) (EDC) is used as a coupling agent. Upon completion (monitored by pNA assay), the excess solvent is removed, and the CPG:sAAPF-pNA is rinsed with dimethyl sulfoxide (DMSO) and doubly-distilled water. This is followed by oven drying with a N_2
20 purge at about 70°C. The reaction scheme and preparation of the immobilized substrate are conducted as described by Brode, P.F. III, and D.S. Rauch, "Subtilisin BPN": Activity on an Immobilized Substrate," LANGMUIR, Vol. 8, p. 1325-1329, (1992), incorporated herein by reference.

The CPG surface will have $62,000 \pm 7,000$ pNA molecules/ μm^2 . The
25 surface area will remain unchanged from the value of $50.0\text{m}^2/\text{g}$ reported by CPG Inc. for the CPG as received. This suggests that the procedure used to add sAAPF-pNA to CPG does not damage the porous structure (mean diameter is 486 Å).

Example 5

Surface Hydrolysis Assay

Using CPG:sAAPF-pNA, adsorption of an enzyme variant and hydrolysis of a CPG-bound peptide can be measured in a single experiment. A small volume of enzyme variant stock solution is added to a flask containing Tris buffer and CPG:sAAPF-pNA which has been degassed. The flask is
35 shaken on a wrist-action shaker for a period of 90 minutes during which the shaker is stopped at various time intervals (for example, every 2 minutes during the early stages of adsorption hydrolysis - e.g., the first 20 minutes - and every 10 minutes towards the end of the experiment). The CPG:sAAPF-

pNA is allowed to settle and the solution is sampled. Both the experimental procedure and the calculation of the adsorption and hydrolysis are conducted as described by Brode et al., 1992, above.

All enzymes are monitored for stability against autolysis and should show no appreciable autolytic loss over the time course of this experiment. Therefore, enzyme adsorption can be determined by measuring solution depletion. The difference between the initial enzyme variant concentration and the concentration measured at each individual time point gives the amount of enzyme variant adsorbed. The amount of pNA hydrolyzed from the surface is measured by taking an absorbance reading on an aliquot of the sample at 410 nm. The total amount of pNA hydrolyzed is calculated by adding the amount sampled and the amount remaining in the flask. This value is corrected by subtracting the amount of pNA that is hydrolyzed by Tris buffer at pH 8.6 when no enzyme is present. This base-hydrolysis ranges from 7-29% of the total hydrolysis depending on the efficiency of the enzyme.

Example 6

Soluble Substrate Kinetic Analysis

The rates of hydrolysis of the soluble substrate sAAPF-pNA are monitored by measuring the absorbance increase as a function of time at 410 nm on a DU-70 spectrophotometer. The enzyme concentration is held constant and is prepared to be in the range of 6-10 nanomolar while the substrate concentration is varied from 90-700 μ M sAAPF-pNA for each kinetic determination. An absorbance data point is taken each second over a period of 900 seconds and the data are transferred to a LOTUS™ spreadsheet (Lotus Development Corporation, Cambridge, Massachusetts). Analysis for kinetic parameters is conducted by the standard Lineweaver Burk analysis in which the data in the initial part of the run (generally the first minute) are fit to a linear regression curve to give v_0 . The v_0 and s_0 data are plotted in the standard inverse fashion to give K_M and k_{cat} .

F. Example Subtilisin 309 Variants

Subtilisin 309 variants of the present invention which have decreased adsorption to and increased hydrolysis of surface bound substrates are exemplified in Tables 3-38, below. In describing the specific mutations, the original amino acid occurring in wild-type is given first, the position number second, and the substituted amino acid third.

TABLE 3

Loop 1 - Single Mutation Variants

Gln57Asn

	Gln57Asp
	Gln57Glu
	Gln57Ser
	Asp58Glu
5	Gly59Asn
	Gly59Asp
	Gly59Gln
	Gly59Glu
	Gly59Pro
10	Gly59Ser
	Asn60Asp
	Asn60Gln
	Asn60Glu
	Asn60Ser
15	Gly61Asn
	Gly61Asp
	Gly61Gln
	Gly61Glu
	Gly61Pro
20	Gly61Ser
	Gly63Asn
	Gly63Asp
	Gly63Gln
	Gly63Glu
25	Gly63Pro
	Gly63Ser
	Thr64Asn
	Thr64Asp
	Thr64Gln
30	Thr64Glu
	Thr64Gly
	Thr64Pro
	Thr64Ser

35

TABLE 4

 Loop 1 - Double Mutation Variants

	Gln57Ser + Asn60Glu
	Asp58Glu + Gly61Gln
	Gly59Ser + Gly63Ser
40	Asn60Ser + Gly61Ser
	Gly63Asn + Thr64Asp
	Gly59Asn + Thr64Glu
	Asn60Glu + Gly63Ser
	Asn60Gln + Gly63Gln
45	Asn60Asp + Gly63Ser
	Asp58Glu + Gly63Gln
	Gln57Asp + Thr64Gly
	Gln57Glu + Gly63Gln
	Asn60Glu + Gly63Asn
50	Gly61Gln + Gly63Asn
	Asp58Glu + Gly59Asn
	Asp58Glu + Thr64Pro

	Gly61Asn + Gly63Asn
	Asp58Glu + Gly61Pro
	Asn60Glu + Gly63Gln
	Asn60Asp + Gly61Gln
5	Asp58Glu + Asn60Ser
	Gln57Asn + Gly59Glu
	Asn60Glu + Gly61Pro
	Gly61Asn + Thr64Gln
	Asp58Glu + Thr64Ser
10	Asn60Asp + Thr64Gln
	Gly59Glu + Gly63Ser
	Gln57Asn + Gly61Ser
	Gly61Ser + Thr64Asn
	Gln57Asp + Gly61Asn
15	Gly59Glu + Gly63Pro
	Asn60Gln + Gly61Ser
	Gly61Pro + Gly63Ser
	Gly59Asp + Gly63Asn
	Gly63Gln + Thr64Asn
20	Gln57Glu + Gly59Gln
	Gln57Asp + Gly59Pro
	Gln57Glu + Gly61Ser
	Gln57Asp + Gly63Gln
	Asp58Glu + Gly61Asn
25	Gly59Asn + Asn60Glu
	Gly61Gln + Thr64Glu
	Gln57Glu + Gly61Gln
	Asp58Glu + Gly63Ser
	Gly59Glu + Gly63Asn
30	Gly61Ser + Thr64Asp
	Gly59Ser + Thr64Asp
	Gln57Glu + Gly63Pro
	Gly59Ser + Thr64Glu
	Asn60Gln + Gly63Pro
35	Gln57Asn + Asn60Asp

TABLE 5

Loop 1 - Triple Mutation Variants	
	Gly59Pro + Gly63Gln + Thr64Glu
40	Gln57Ser + Gly59Asn + Gly63Pro
	Gly59Pro + Asn60Asp + Thr64Asn
	Gln57Glu + Gly59Asn + Gly63Pro
	Gln57Asp + Gly63Pro + Thr64Asn
	Gln57Ser + Asn60Glu + Thr64Gly
45	Gln57Ser + Asn60Ser + Gly63Ser
	Gly61Ser + Gly63Ser + Thr64Gln
	Gln57Glu + Gly61Pro + Thr64Gly
	Asp58Glu + Gly63Pro + Thr64Gly
	Gln57Asn + Asp58Glu + Gly61Pro
50	Asp58Glu + Gly59Ser + Thr64Pro
	Gln57Asn + Gly59Glu + Gly61Ser
	Gly59Glu + Gly61Gln + Thr64Asn

	Gln57Asp + Asn60Gln + Thr64Gly
	Asn60Glu + Gly61Gln + Thr64Gly
	Gln57Asp + Gly59Pro + Gly63Pro
	Gln57Asn + Gly63Asn + Thr64Gly
5	Gln57Ser + Gly59Asp + Gly61Ser
	Gly61Gln + Gly63Asn + Thr64Pro
	Gln57Glu + Gly59Pro + Thr64Ser
	Asn60Asp + Gly63Gln + Thr64Gly
	Asp58Glu + Gly63Asn + Thr64Gln
10	Asp58Glu + Gly61Gln + Gly63Gln
	Gln57Asp + Gly61Pro + Thr64Gln
	Asp58Glu + Gly59Asn + Gly61Ser
	Asp58Glu + Gly59Ser + Asn60Ser
	Gln57Asn + Gly61Pro + Thr64Gly
15	Gly59Glu + Gly61Pro + Gly63Pro
	Gly59Glu + Gly61Gln + Gly63Asn
	Gly59Glu + Gly61Pro + Gly63Gln
	Gly59Glu + Gly61Pro + Thr64Asn
	Gln57Asn + Asp58Glu + Thr64Gln

20

TABLE 6

Loop 1 - Quadruple Mutation Variants

	Gly59Gln + Asn60Asp + Gly61Pro + Gly63Pro
	Gly59Ser + Asn60Gln + Gly63Ser + Thr64Asp
25	Gly59Pro + Asn60Ser + Gly61Ser + Gly63Gln
	Gln57Glu + Gly59Pro + Asn60Ser + Gly61Pro
	Gln57Glu + Asn60Gln + Gly63Asn + Thr64Gly
	Gln57Ser + Gly59Ser + Asn60Asp + Gly61Ser
	Gln57Ser + Asn60Glu + Gly61Pro + Thr64Pro
30	Asn60Gln + Gly61Pro + Gly63Gln + Thr64Asp
	Asn60Glu + Gly61Gln + Gly63Asn + Thr64Pro
	Gln57Glu + Gly59Gln + Gly61Pro + Thr64Gln
	Gln57Asn + Asp58Glu + Gly59Ser + Asn60Gln
	Asp58Glu + Asn60Ser + Gly63Ser + Thr64Ser
35	Gln57Glu + Gly59Pro + Gly63Gln + Thr64Ser
	Asp58Glu + Gly59Ser + Asn60Ser + Gly63Ser
	Gly59Asn + Asn60Asp + Gly61Ser + Thr64Gln
	Gln57Glu + Asp58Glu + Gly59Gln + Gly61Gln
	Gln57Glu + Asp58Glu + Asn60Ser + Thr64Pro
40	Gln57Asp + Asp58Glu + Gly61Ser + Gly63Pro
	Gln57Asp + Asp58Glu + Asn60Gln + Gly61Gln
	Gln57Ser + Asp58Glu + Gly59Glu + Asn60Gln
	Asp58Glu + Gly59Asp + Gly61Ser + Gly63Gln
	Gly59Glu + Asn60Asp + Gly61Asn + Gly63Asn
45	Gly59Asp + Asn60Asp + Gly61Asn + Gly63Gln
	Gly59Glu + Asn60Asp + Gly61Pro + Thr64Ser
	Asp58Glu + Gly59Glu + Asn60Asp + Thr64Gly
	Asp58Glu + Gly59Glu + Asn60Asp + Gly61Pro
	Asp58Glu + Gly59Glu + Asn60Glu + Gly61Asn

50

TABLE 7

Loop 2 - Single Mutation Variants	
5	Val 93Ala
	Val 93Asn
	Val 93Asp
	Val 93Cys
	Val 93Gln
10	Val 93Glu
	Val 93Gly
	Val 93His
	Val 93Met
	Val 93Pro
15	Val 93Ser
	Val 93Thr
	Leu 94Ala
	Leu 94Asn
	Leu 94Asp
20	Leu 94Cys
	Leu 94Gln
	Leu 94Glu
	Leu 94Gly
	Leu 94His
25	Leu 94Ile
	Leu 94Met
	Leu 94Pro
	Leu 94Ser
	Leu 94Thr
30	Leu 94Val
	Gly 95Asn
	Gly 95Asp
	Gly 95Gln
	Gly 95Glu
35	Gly 95Pro
	Gly 95Ser
	Ala 96Asn
	Ala 96Asp
	Ala 96Gln
40	Ala 96Glu
	Ala 96Gly
	Ala 96His
	Ala 96Pro
	Ala 96Ser
45	Ala 96Thr
	Ser 97Asp
	Ser 97Glu
	Gly 98Asn
	Gly 98Asp
50	Gly 98Gln
	Gly 98Glu
	Gly 98Pro
	Gly 98Ser
	Ser 99Asp
	Ser 99Glu

26

	Gly100Asn
	Gly100Asp
	Gly100Gln
	Gly100Glu
5	Gly100Pro
	Gly100Ser
	Ser101Asp
	Ser101Glu
	Val102Ala
10	Val102Asn
	Val102Asp
	Val102Cys
	Val102Gln
	Val102Glu
15	Val102Gly
	Val102His
	Val102Met
	Val102Pro
	Val102Ser
20	Val102Thr
	Ser103Asp
	Ser103Glu
	Ser104Asp
	Ser104Glu
25	Ile105Ala
	Ile105Asn
	Ile105Asp
	Ile105Cys
	Ile105Gln
30	Ile105Glu
	Ile105Gly
	Ile105His
	Ile105Leu
	Ile105Met
35	Ile105Pro
	Ile105Ser
	Ile105Thr
	Ile105Val

TABLE 8

Loop 2 - Double Mutation Variants

	Val 93Gln + Ser 99Glu
	Gly 95Ser + Gly 98Gln
	Ser101Asp + Ile105Ala
45	Leu 94Ser + Gly 95Ser
	Leu 94Pro + Ser101Asp
	Gly 98Gln + Ser103Asp
	Ser 97Asp + Tyr102Gln
	Tyr102Cys + Ile105Met
50	Val 93Pro + Gly 98Gln
	Ser 99Glu + Gly100Pro
	Ser103Asp + Ile105Leu

	Ser 97Asp + Gly 98Gln
	Val 93Ser + Ser 99Asp
	Leu 94Ser + Gly 98Glu
	Gly 95Glu + Tyr102Met
5	Gly 95Asn + Ser103Glu
	Gly 98Ser + Tyr102Thr
	Gly 98Gln + Tyr102Cys
	Leu 94Ile + Ile105Gln
	Leu 94Asp + Gly100Gln
10	Ala 96Gly + Ser101Asp
	Ser101Glu + Ile105Gln
	Gly 95Gln + Ile105Ser
	Val 93Gln + Gly100Pro
	Val 93Met + Ser104Asp
15	Gly 98Pro + Ser101Asp
	Val 93Pro + Ile105His
	Gly 95Asp + Gly100Ser
	Tyr102Cys + Ile105Leu
	Gly100Asn + Ile105Met
20	Gly 98Asn + Ser101Glu
	Ser 99Glu + Ile105Gln
	Val 93Thr + Tyr102Thr
	Gly 98Ser + Ser104Glu
	Gly 95Asn + Ser104Glu
25	Val 93Pro + Ser103Glu
	Gly 95Asn + Tyr102Ile
	Leu 94Pro + Gly 98Asp
	Leu 94His + Gly 98Asp
	Val 93Asn + Tyr102Thr
30	Tyr102Ala + Ser103Asp
	Gly 98Pro + Ser103Glu
	Leu 94Cys + Tyr102Leu
	Val 93Gly + Gly 98Ser
	Gly100Gln + Tyr102Ser
35	Val 93Thr + Gly100Asn
	Gly 98Asn + Ile105Pro
	Val 93Asp + Leu 94Ala
	Leu 94Gly + Ser104Glu
	Val 93Met + Ser101Asp
40	Val 93Met + Ser 97Glu
	Ala 96Pro + Ile105Asn
	Ser 97Glu + Gly 98Pro
	Ala 96Thr + Ser 99Glu
	Val 93Asn + Gly100Asn
45	Gly 95Gln + Gly 98Pro
	Gly 95Asn + Ala 96His
	Val 93Ser + Ser103Asp
	Gly 98Gln + Ile105Pro
	Val 93Cys + Ile105Glu

TABLE 9

		Loop 2 - Triple Mutation Variants		
5		Val 93Gln + Leu 94Thr + Ser 99Glu		
		Leu 94Met + Gly 95Gln + Ser104Asp		
		Ser 99Glu + Tyr102Met + Ile105Thr		
		Val 93Thr + Leu 94Thr + Ile105Cys		
		Leu 94Asp + Ala 96Thr + Gly 98Asn		
10		Val 93Met + Gly 95Gln + Ser103Asp		
		Val 93Cys + Ala 96Pro + Ser 99Glu		
		Leu 94Asp + Ala 96Gly + Gly100Gln		
		Leu 94His + Gly 98Gln + Ser 99Glu		
		Gly 95Pro + Ser101Asp + Tyr102Gln		
15		Leu 94Asn + Gly 95Gln + Ser101Asp		
		Leu 94His + Gly 98Pro + Ser104Glu		
		Leu 94Thr + Ala 96Asn + Gly100Pro		
		Gly 95Ser + Gly 98Ser + Tyr102Glu		
		Ala 96Thr + Ser 97Asp + Tyr102Thr		
20		Leu 94Asn + Gly100Ser + Ser101Glu		
		Leu 94Met + Gly 98Gln + Gly100Asn		
		Val 93Pro + Ala 96Glu + Ile105Ala		
		Val 93Cys + Gly 95Glu + Tyr102Leu		
		Leu 94Cys + Gly 95Ser + Ser 97Asp		
25		Gly 95Gln + Ser101Glu + Tyr102His		
		Val 93Gln + Gly 95Glu + Ile105Gln		
		Val 93Gly + Ser 99Asp + Ile105Gly		
		Gly 95Asn + Gly 98Glu + Ile105Val		
		Ser 97Glu + Gly 98Pro + Tyr102Thr		
30		Val 93Glu + Leu 94Ile + Gly100Gln		
		Ala 96Pro + Ser101Asp + Ile105Pro		
		Gly 98Pro + Ser103Asp + Ile105Val		
		Ala 96Gln + Ser 99Asp + Tyr102Ser		
		Ser 97Asp + Gly 98Ser + Ile105Asn		
35		Val 93Gln + Gly 98Asn + Tyr102Leu		
		Leu 94Gly + Tyr102Pro + Ser103Glu		
		Val 93Thr + Gly100Gln + Ser104Glu		
		Val 93Gly + Gly100Gln + Ser103Glu		
		Ala 96Thr + Gly100Ser + Ser103Glu		
40		Gly100Asn + Ser101Glu + Ile105Thr		
		Gly 95Asp + Tyr102Gly + Ile105Met		
		Val 93Cys + Ala 96Thr + Ile105Cys		
		Ala 96Gly + Gly 98Asp + Ser 99Asp		
		Gly 95Ser + Ser 97Asp + Gly 98Asp		
45		Leu 94Asn + Ser103Glu + Ser104Asp		
		Tyr102Val + Ser103Glu + Ser104Glu		
		Ser 99Asp + Gly100Glu + Ile105Met		
		Ser 97Asp + Gly 98Asp + Ser 99Glu		
		Gly 95Asn + Ser101Glu + Ser103Glu		
50		Ser101Glu + Tyr102Asn + Ser103Glu		
		Leu 94Asp + Ser 99Glu + Gly100Gln		
		Gly100Asp + Ser101Glu + Ser104Glu		
		Leu 94Asp + Gly 98Glu + Ile105Cys		
		Gly 95Glu + Ser 97Glu + Tyr102Asn		
		Tyr102Thr + Ser103Glu + Ile105Glu		

Gly 95Asp + Ser 99Glu + Gly100Gln
 Gly 95Glu + Ser 99Glu + Tyr102Met
 Val 93Gln + Ser 97Asp + Ser 99Glu
 Gly100Glu + Ser101Asp + Ser103Asp
 5 Val 93Asp + Ser103Glu + Ser104Glu
 Val 93Asp + Ser 99Asp + Gly100Asp
 Ala 96Gln + Gly100Asp + Ser104Asp
 Val 93Asp + Ser101Glu + Ile105Asp
 Leu 94Asp + Ser 99Glu + Ser101Glu

10

TABLE 10

Loop 2 - Quadruple Mutation Variants	
	Leu 94Asn + Ser 97Glu + Tyr102Asn + Ile105Met
	Leu 94Pro + Gly 95Glu + Gly100Gln + Tyr102Ala
15	Val 93Cys + Leu 94Met + Gly 95Pro + Ala 96Gln
	Gly 95Pro + Ser 97Glu + Tyr102Gln + Ile105Leu
	Gly 95Asp + Gly100Pro + Tyr102Val + Ile105Cys
	Ala 96Thr + Gly100Asp + Tyr102Ala + Ile105Asn
	Val 93Asn + Leu 94Cys + Ser101Asp + Tyr102Val
20	Val 93Asn + Gly 95Asn + Ser104Asp + Ile105Val
	Leu 94Ser + Gly 98Pro + Ser103Glu + Ile105Val
	Val 93Asn + Leu 94His + Gly 95Asn + Ile105Asn
	Ala 96Ser + Gly 98Asn + Ser 99Glu + Tyr102Gly
	Val 93Asn + Gly 98Asn + Tyr102Ile + Ile105Asp
25	Val 93Asn + Tyr102Asn + Ser103Asp + Ile105Ser
	Ala 96Ser + Gly100Ser + Ser101Asp + Tyr102Pro
	Leu 94Pro + Ala 96Ser + Ser101Asp + Tyr102Ser
	Val 93Met + Ala 96Thr + Ser104Asp + Ile105Gln
	Val 93Met + Leu 94Ala + Gly 95Pro + Ser104Glu
30	Val 93Cys + Gly 95Pro + Ala 96Glu + Tyr102Val
	Gly 95Asn + Ala 96Asn + Ser104Glu + Ile105Pro
	Val 93Asn + Leu 94Asn + Gly 98Glu + Ser 99Glu
	Leu 94His + Gly 98Glu + Ser 99Glu + Tyr102Ser
	Gly 95Pro + Gly 98Glu + Ser 99Asp + Ile105Gly
35	Val 93Ala + Ala 96Ser + Ser103Glu + Ser104Glu
	Leu 94Gly + Ser 97Asp + Gly 98Asp + Ser 99Glu
	Val 93Cys + Leu 94Asp + Gly 95Asn + Gly100Glu
	Val 93Ser + Ser101Glu + Ser103Asp + Ser104Asp
	Ala 96Ser + Ser101Glu + Tyr102Gln + Ser103Asp
40	Val 93Thr + Gly100Asn + Ser101Glu + Ser103Asp
	Val 93Asn + Leu 94Glu + Gly 95Glu + Ser 99Glu
	Leu 94Asp + Ala 96Gly + Ser 99Glu + Ile105Cys
	Leu 94Ala + Ser101Glu + Ser104Asp + Ile105Ser
	Ala 96His + Ser101Glu + Ser104Glu + Ile105Ala
45	Val 93Gly + Gly100Pro + Ser101Glu + Ser104Asp
	Gly 95Gln + Ser101Glu + Ser104Asp + Ile105Met
	Gly 98Gln + Ser101Glu + Ser104Glu + Ile105Asn
	Val 93Gly + Ser101Asp + Tyr102Glu + Ile105Asp
	Ser101Asp + Tyr102Val + Ser104Glu + Ile105Glu
50	Val 93Cys + Gly 95Asp + Gly 98Asp + Gly100Pro
	Gly 95Asp + Ser 97Glu + Tyr102Ala + Ile105Cys
	Val 93Thr + Gly 95Glu + Ala 96Asn + Ser 99Asp

	Val 93Cys + Gly 95Asp + Ser 99Glu + Ile105Val
	Val 93Cys + Ser101Asp + Ser103Glu + Ile105Asp
	Ala 96His + Ser 97Glu + Ser 99Asp + Ile105Asn
	Ala 96Asn + Ser 97Glu + Ser 99Glu + Tyr102Pro
5	Val 93Cys + Ser 97Glu + Ser 99Asp + Ile105His
	Val 93Ser + Ser 97Glu + Gly 98Gln + Ser 99Glu
	Gly 95Asn + Ser 97Asp + Ser 99Glu + Gly100Glu
	Val 93Met + Gly100Asp + Tyr102Asp + Ser103Asp
	Leu 94Gly + Ser101Asp + Tyr102Ala + Ile105Glu
10	Ser 97Glu + Gly 98Asp + Gly100Asp + Tyr102Gly
	Leu 94Ser + Ser 99Glu + Gly100Glu + Ser104Glu
	Val 93Asn + Ser 99Glu + Gly100Glu + Ser104Asp
	Val 93Ala + Ser 99Glu + Gly100Asp + Ser104Asp
	Leu 94Cys + Gly 95Ser + Ser 99Asp + Ser101Glu
15	Gly 95Ser + Ala 96Thr + Ser 99Glu + Ser101Asp
	Leu 94Cys + Ala 96Ser + Ser 99Asp + Ser101Asp
	Ser 99Asp + Ser101Glu + Tyr102Asn + Ile105Val
	Val 93Glu + Gly 95Pro + Ser101Glu + Ser103Asp
	Val 93Ala + Gly 95Asp + Ser 99Asp + Ser101Glu
20	Ser 99Glu + Ser101Glu + Tyr102Pro + Ser104Glu

TABLE 11

Loop 3 - Single Mutation Variants

	Leu124Ala
25	Leu124Asn
	Leu124Asp
	Leu124Cys
	Leu124Gln
	Leu124Glu
30	Leu124Gly
	Leu124His
	Leu124Ile
	Leu124Met
	Leu124Pro
35	Leu124Ser
	Leu124Thr
	Leu124Val
	Gly125Asn
	Gly125Asp
40	Gly125Gln
	Gly125Glu
	Gly125Pro
	Gly125Ser
	Ser126Asp
45	Ser126Glu
	Pro127Asn
	Pro127Asp
	Pro127Gln
	Pro127Glu
50	Pro127Gly
	Pro127Ser
	Ser128Asp

	Ser128Glu
	Pro129Asn
	Pro129Asp
	Pro129Gln
5	Pro129Glu
	Pro129Gly
	Pro129Ser
	Ser130Asp
	Ser130Glu
10	Ala131Asn
	Ala131Asp
	Ala131Gln
	Ala131Glu
	Ala131Gly
15	Ala131His
	Ala131Pro
	Ala131Ser
	Ala131Thr

20

TABLE 12

Loop 3 - Double Mutation Variants

	Leu124Gln + Ser128Glu
	Gly125Ser + Ser126Glu
	Gly125Ser + Ser128Glu
25	Pro127Gly + Ser130Glu
	Leu124Thr + Ser126Glu
	Ser126Glu + Pro129Ser
	Gly125Gln + Ser128Glu
	Pro127Ser + Ser130Glu
30	Gly125Glu + Pro127Asn
	Pro129Gln + Ser130Glu
	Gly125Asp + Ala131His
	Pro127Gly + Ala131Glu
	Leu124His + Ser126Asp
35	Pro127Gly + Pro129Asp
	Ser126Glu + Ala131Gln
	Leu124Asp + Ala131Pro
	Gly125Pro + Pro127Glu
	Gly125Ser + Ser126Asp
40	Leu124Gln + Ala131Asn
	Gly125Asp + Pro129Ser
	Pro129Asn + Ala131Asp
	Pro127Asn + Ser128Asp
	Pro129Gly + Ala131Glu
45	Pro127Ser + Pro129Asp
	Pro127Ser + Ser128Glu
	Leu124Gly + Ser130Glu
	Gly125Asn + Ser130Asp
	Leu124Glu + Pro127Asn
50	Ser130Glu + Ala131Gly
	Ser130Asp + Ala131Thr
	Leu124Gln + Ser128Asp

	Leu124Ser + Ala131Pro
	Pro129Ser + Ser130Glu
	Gly125Gln + Pro127Asp
	Leu124Cys + Ala131Thr
5	Gly125Gln + Pro129Gln
	Leu124Met + Ala131Gln
	Gly125Gln + Ala131Asp
	Ser128Glu + Ala131Asn
	Ser130Glu + Ala131Pro
10	Gly125Pro + Ala131Ser
	Pro127Ser + Pro129Asn
	Ser126Glu + Pro127Gln
	Pro127Ser + Ser130Asp
	Pro127Gly + Ser128Asp
15	Gly125Glu + Pro127Ser
	Leu124Cys + Pro129Asn
	Gly125Gln + Pro129Glu
	Gly125Asn + Ala131Asp
	Gly125Ser + Pro129Gln
20	Ser126Asp + Pro129Gln
	Leu124Val + Pro129Asn
	Leu124His + Ser126Glu
	Pro127Glu + Ala131Gly
	Leu124Thr + Gly125Pro
25	Leu124His + Ser130Glu
	Gly125Asn + Ser126Asp
	Pro129Asn + Ala131Pro
	Pro127Gln + Pro129Asn
	Leu124Gly + Pro129Glu

30

TABLE 13

Loop 3 - Triple Mutation Variants	
	Gly125Gln + Ser126Glu + Ala131His
	Ser126Asp + Pro127Ser + Ala131His
35	Leu124Val + Ser130Asp + Ala131Asn
	Leu124Gln + Ser126Glu + Ala131Ser
	Gly125Ser + Pro129Glu + Ala131Gly
	Leu124Ser + Pro127Asp + Ala131Gln
	Pro127Ser + Ser128Asp + Ala131His
40	Leu124Thr + Pro127Glu + Ala131Ser
	Leu124Gln + Ser126Glu + Ala131Asn
	Gly125Asn + Pro127Glu + Ala131Gln
	Gly125Gln + Ser126Asp + Pro127Gln
	Pro127Asn + Ser130Asp + Ala131Thr
45	Gly125Asn + Pro127Glu + Pro129Asn
	Leu124Thr + Ser128Asp + Ala131Gln
	Gly125Ser + Pro129Gln + Ala131Glu
	Pro127Gln + Pro129Asn + Ser130Glu
	Leu124Ile + Gly125Gln + Ser130Glu
50	Pro129Asn + Ser130Glu + Ala131Gly
	Leu124Ser + Gly125Ser + Pro129Gln
	Leu124Asn + Gly125Gln + Ser128Asp

	Leu124Gln + Pro127Ser + Ser130Asp
	Gly125Ser + Pro127Ser + Ala131Asp
	Gly125Ser + Ser128Glu + Pro129Gln
	Pro127Asn + Ser128Asp + Ala131Gly
5	Leu124Thr + Gly125Ser + Ala131Asn
	Gly125Gln + Pro129Ser + Ser130Asp
	Gly125Pro + Ser126Glu + Pro129Asn
	Pro129Gly + Ser130Asp + Ala131Pro
	Gly125Asn + Ser126Asp + Pro129Gly
10	Gly125Asp + Ser126Asp + Ala131Asn
	Gly125Glu + Ser126Glu + Ala131Ser
	Gly125Glu + Ser126Asp + Ala131His
	Gly125Gln + Ser128Glu + Pro129Glu
	Ser128Glu + Pro129Glu + Ala131Gly
15	Leu124Cys + Ser128Glu + Pro129Asp
	Pro127Gly + Ser128Glu + Pro129Glu
	Pro127Gly + Ser128Asp + Pro129Asp
	Leu124Asn + Ser128Glu + Pro129Asp
	Ser126Glu + Pro127Asp + Ala131Asn
20	Ser126Glu + Pro127Glu + Pro129Gly
	Leu124His + Ser126Asp + Pro127Glu
	Ser126Asp + Pro127Glu + Pro129Gly
	Pro127Asp + Ser128Asp + Pro129Asn
	Pro127Asp + Ser128Glu + Ala131His
25	Pro127Glu + Ser128Asp + Ala131Pro
	Leu124Ile + Pro127Glu + Ser128Glu
	Pro129Asp + Ser130Asp + Ala131Gly
	Leu124Pro + Pro129Glu + Ser130Glu
	Ser126Asp + Pro127Glu + Ser128Asp
30	Ser126Glu + Pro127Asp + Ser128Asp
	Pro129Glu + Ser130Asp + Ala131Glu
	Leu124Asp + Gly125Asp + Ser126Asp
	Leu124Ser + Ser126Asp + Ser128Asp
	Ser126Glu + Ser128Asp + Pro129Asn
35	Gly125Asn + Ser126Glu + Ser128Glu
	Ser126Glu + Ser128Glu + Ala131Thr
	Leu124Asn + Ser126Glu + Ser128Glu
	Ser126Glu + Ser128Glu + Pro129Glu
	Gly125Glu + Ser126Glu + Ser128Asp
40	Ser128Asp + Pro129Ser + Ser130Glu

TABLE 14

Loop 3 - Quadruple Mutation Variants

	Gly125Gln + Ser126Glu + Pro127Ser + Ala131Ser
45	Gly125Asn + Pro127Ser + Ser130Asp + Ala131Asn
	Leu124Ala + Pro127Gln + Ser128Glu + Ala131Pro
	Gly125Pro + Pro127Ser + Pro129Ser + Ser130Glu
	Gly125Asn + Pro129Asn + Ser130Asp + Ala131Gln
	Gly125Asn + Pro129Asn + Ser130Glu + Ala131Pro
50	Leu124Ser + Ser126Glu + Pro129Gly + Ala131Gln
	Gly125Asn + Ser126Glu + Pro127Gly + Ala131Ser
	Leu124Ile + Ser126Asp + Pro129Gln + Ala131Ser

	Leu124His + Gly125Ser + Pro129Gly + Ala131Asn
	Leu124Ala + Gly125Glu + Pro127Gln + Pro129Gln
	Leu124Ser + Gly125Glu + Ser126Asp + Pro129Ser
	Gly125Glu + Ser126Glu + Pro127Gln + Ala131His
5	Leu124Met + Gly125Asp + Ser126Asp + Pro127Asn
	Leu124Gln + Ser128Glu + Pro129Asp + Ala131Gln
	Leu124Val + Ser128Glu + Pro129Glu + Ala131Asn
	Pro127Ser + Ser128Asp + Pro129Asp + Ala131Thr
	Leu124Ile + Ser128Glu + Pro129Asp + Ala131Ser
10	Gly125Ser + Ser126Glu + Pro127Glu + Ala131Gln
	Leu124His + Gly125Gln + Ser130Glu + Ala131Glu
	Leu124Thr + Gly125Gln + Ser130Asp + Ala131Asp
	Leu124His + Pro127Glu + Ser128Glu + Ala131His
	Gly125Ser + Pro127Asp + Ser128Asp + Pro129Gln
15	Leu124Asn + Ser126Glu + Pro127Asp + Ser128Asp
	Pro127Gln + Ser128Glu + Pro129Asp + Ser130Asp
	Gly125Pro + Ser128Asp + Pro129Glu + Ser130Glu
	Leu124Asn + Gly125Asp + Ser126Asp + Pro127Asp
	Leu124Asp + Gly125Asp + Ser126Asp + Pro129Gln
20	Leu124Asp + Gly125Glu + Ser126Asp + Pro129Gly
	Gly125Gln + Ser126Glu + Ser128Glu + Ala131Thr
	Leu124Asn + Ser126Glu + Pro127Gln + Ser128Asp
	Leu124Met + Gly125Pro + Ser126Asp + Ser128Glu
	Leu124Asn + Gly125Ser + Ser126Asp + Ser128Asp
25	Leu124Val + Ser126Glu + Ser128Glu + Pro129Asp
	Leu124Cys + Ser126Asp + Ser128Glu + Pro129Glu
	Ser126Asp + Pro127Asp + Pro129Glu + Ala131Ser
	Gly125Asn + Ser126Glu + Pro127Glu + Pro129Glu
	Leu124Ser + Ser126Asp + Pro127Asp + Pro129Asp
30	Gly125Asp + Ser126Glu + Ser128Asp + Pro129Ser
	Leu124Val + Gly125Asp + Ser126Glu + Ser128Glu
	Gly125Glu + Ser126Glu + Ser128Asp + Pro129Asn
	Gly125Glu + Ser126Asp + Pro127Ser + Ser128Asp
	Leu124Met + Ser128Glu + Ser130Glu + Ala131Ser
35	Leu124Cys + Ser128Glu + Pro129Ser + Ser130Asp
	Gly125Gln + Ser128Glu + Ser130Glu + Ala131His
	Leu124Met + Pro127Gln + Ser128Glu + Ser130Glu
	Leu124Gly + Ser126Asp + Pro129Glu + Ser130Asp
	Gly125Asn + Ser126Glu + Pro129Glu + Ser130Glu
40	Leu124Gly + Gly125Asp + Pro127Asp + Pro129Gly
	Ser126Asp + Ser128Asp + Ser130Glu + Ala131Gln
	Gly125Pro + Ser126Asp + Ser128Glu + Ser130Asp
	Ser126Asp + Pro127Gly + Ser128Glu + Ser130Glu
	Ser126Glu + Pro127Gly + Ser128Asp + Ser130Glu
45	Ser126Asp + Ser128Asp + Pro129Ser + Ser130Asp
	Ser126Glu + Ser128Asp + Ser130Asp + Ala131His
	Ser126Glu + Ser128Glu + Ser130Glu + Ala131Ser
	Gly125Pro + Ser126Glu + Ser128Glu + Ser130Asp
	Leu124Val + Ser126Asp + Ser128Glu + Ser130Asp
50	Gly125Gln + Ser126Glu + Ser128Asp + Ser130Glu
	Ser126Glu + Ser128Asp + Pro129Gly + Ser130Glu

TABLE 15

Loop 4 - Single Mutation Variants	
5	Gly152Asn
	Gly152Asp
	Gly152Gln
	Gly152Glu
	Gly152Pro
10	Gly152Ser
	Asn153Asp
	Asn153Gln
	Asn153Glu
	Asn153Ser
15	Ser154Asp
	Ser154Glu
	Gly155Asn
	Gly155Asp
	Gly155Gln
20	Gly155Glu
	Gly155Pro
	Gly155Ser
	Ala156Asn
	Ala156Asp
25	Ala156Gln
	Ala156Glu
	Ala156Gly
	Ala156His
	Ala156Pro
30	Ala156Ser
	Ala156Thr
	Gly157Asn
	Gly157Asp
	Gly157Gln
35	Gly157Glu
	Gly157Pro
	Gly157Ser
	Ser158Asp
	Ser158Glu
40	Ile159Ala
	Ile159Asn
	Ile159Asp
	Ile159Cys
	Ile159Gln
45	Ile159Glu
	Ile159Gly
	Ile159His
	Ile159Leu
	Ile159Met
50	Ile159Pro
	Ile159Ser
	Ile159Thr
	Ile159Val
	Ser160Asp
	Ser160Glu

	Tyr161Ala
	Tyr161Asn
	Tyr161Asp
	Tyr161Cys
5	Tyr161Gln
	Tyr161Glu
	Tyr161Gly
	Tyr161His
	Tyr161Ile
10	Tyr161Leu
	Tyr161Met
	Tyr161Pro
	Tyr161Ser
	Tyr161Thr
15	Tyr161Val

TABLE 16

	Loop 4 - Double Mutation Variants
20	Ser154Glu + Gly155Asn
	Ser154Asp + Gly157Gln
	Ser154Glu + Ile159His
	Gly152Gln + Gly157Asp
	Ser154Glu + Gly155Ser
25	Asn153Ser + Ser154Glu
	Ala156Asn + Ser160Glu
	Ala156Thr + Ser158Glu
	Asn153Glu + Gly157Ser
	Gly155Asn + Ala156Asp
	Ile159Gly + Tyr161Gly
30	Gly155Ser + Tyr161Glu
	Ser154Asp + Gly155Pro
	Gly155Asp + Ala156Ser
	Gly152Glu + Asn153Ser
	Ser158Glu + Ile159Asn
35	Asn153Asp + Ala156His
	Ser154Glu + Tyr161Cys
	Ile159Leu + Tyr161Asn
	Gly157Asp + Ile159Gly
	Ser158Asp + Ile159Gly
40	Gly152Pro + Gly155Glu
	Gly155Gln + Ser160Asp
	Gly152Asp + Tyr161Met
	Ser154Glu + Gly155Gln
	Gly155Glu + Tyr161Ala
45	Ala156Ser + Ser160Asp
	Ala156Glu + Tyr161Leu
	Gly152Pro + Gly157Asn
	Ser158Glu + Ile159Ser
	Gly157Asp + Tyr161Thr
50	Ser158Asp + Ile159Cys
	Gly155Pro + Tyr161Ala
	Gly152Asp + Tyr161Ala

	Ala156His + Ile159Asn
	Ser154Asp + Ala156His
	Gly157Pro + Ser158Asp
	Asn153Ser + Ile159Cys
5	Ser154Asp + Ala156Ser
	Ser154Glu + Tyr161Ala
	Ile159Leu + Tyr161Ala
	Gly152Glu + Gly155Gln
	Ala156Pro + Gly157Glu
10	Asn153Asp + Tyr161His
	Ala156Gln + Ile159Asn
	Gly152Pro + Ser154Asp
	Gly155Gln + Ala156Asp
	Ala156Ser + Ile159Gly
15	Asn153Asp + Gly157Gln
	Ile159Leu + Ser160Asp
	Gly155Glu + Ile159Gln
	Ser160Asp + Tyr161Thr
	Ser158Asp + Ile159Gln
20	Ser154Glu + Gly157Asn
	Ala156Gly + Ile159His
	Ala156Ser + Ser158Asp
	Asn153Gln + Gly155Glu
	Gly155Asn + Ser158Glu
25	Ser158Glu + Ile159Pro
	Ser158Asp + Ile159Leu

TABLE 17

Loop 4 - Triple Mutation Variants	
30	Ala156Asn + Gly157Asn + Tyr161Cys
	Gly152Gln + Gly155Glu + Tyr161Asn
	Gly152Gln + Asn153Gln + Ser154Glu
	Gly155Ser + Ser158Glu + Tyr161Gln
	Gly152Glu + Asn153Ser + Ala156Ser
35	Gly152Glu + Ile159Pro + Tyr161Asn
	Gly152Asp + Gly157Gln + Tyr161Met
	Gly155Asn + Ile159Thr + Tyr161His
	Asn153Ser + Gly155Ser + Ser158Glu
	Gly152Ser + Gly155Pro + Ser158Glu
40	Gly152Pro + Gly157Gln + Ser160Asp
	Gly152Gln + Ser154Asp + Tyr161Met
	Ala156Pro + Ile159Asn + Tyr161Ile
	Ile159Asn + Ser160Glu + Tyr161Ser
	Gly152Asp + Ile159Ala + Tyr161Cys
45	Asn153Gln + Ile159Ala + Ser160Glu
	Asn153Asp + Gly155Pro + Tyr161Asn
	Gly155Asn + Ala156Thr + Ser158Asp
	Gly152Gln + Ser154Asp + Tyr161Gln
	Gly157Ser + Ser158Asp + Tyr161Pro
50	Ser154Glu + Gly155Ser + Ile159Cys
	Gly155Gln + Ala156Asn + Ser158Asp
	Gly155Asn + Gly157Asn + Ile159Ala

	Gly157Asn + Ser158Glu + Ile159His
	Asn153Ser + Ile159Leu + Ser160Glu
	Ala156Gln + Gly157Asp + Tyr161Asn
	Gly155Asn + Ala156His + Tyr161Val
5	Asn153Gln + Ala156Asp + Ile159Gly
	Ala156His + Ser160Glu + Tyr161His
	Ala156Gln + Ser160Asp + Tyr161Ala
	Gly152Asp + Gly157Gln + Ile159Gly
	Asn153Glu + Ala156Pro + Ile159Ala
10	Gly152Gln + Gly155Asn + Ala156Thr
	Asn153Gln + Ile159Met + Ser160Glu
	Gly152Asp + Ala156Pro + Tyr161Cys
	Gly152Ser + Ser154Glu + Tyr161Val
	Gly155Asp + Gly157Ser + Tyr161Asn
15	Asn153Glu + Ser154Asp + Gly155Ser
	Asn153Glu + Ser154Asp + Ala156Pro
	Gly157Asn + Ser160Asp + Tyr161Asp
	Gly152Glu + Asn153Asp + Tyr161Met
	Gly152Asp + Asn153Asp + Ile159Leu
20	Ala156Asp + Gly157Glu + Tyr161Thr
	Asn153Ser + Ser154Glu + Gly155Asp
	Ser154Asp + Gly155Asp + Ala156Pro
	Asn153Ser + Ser154Asp + Gly155Glu
	Ser154Glu + Gly155Asp + Tyr161Ala
25	Gly157Asp + Ser158Glu + Tyr161Met
	Gly155Gln + Gly157Asp + Ser158Glu
	Ala156His + Gly157Glu + Ser158Asp
	Gly155Asp + Ala156Glu + Gly157Asp
	Ser154Asp + Ala156Glu + Tyr161Cys
30	Ser154Asp + Ala156Glu + Ile159Pro
	Ser154Asp + Ala156Glu + Ile159Asn
	Gly152Pro + Ala156Glu + Ser158Glu
	Gly155Asn + Ala156Glu + Ser158Glu
	Asn153Glu + Gly155Asp + Ile159Pro
35	Gly152Glu + Ile159Cys + Ser160Asp
	Gly152Glu + Ser154Glu + Gly157Gln
	Gly152Glu + Ser154Glu + Gly155Asn

TABLE 18

Loop 4 - Quadruple Mutation Variants	
40	Ala156Pro + Ile159Pro + Ser160Glu + Tyr161Thr
	Asn153Gln + Gly157Asn + Ile159Gln + Ser160Asp
	Asn153Gln + Ala156Gly + Gly157Glu + Ile159Asn
	Gly152Asn + Ile159Gln + Ser160Asp + Tyr161Met
45	Gly152Pro + Ser154Glu + Gly157Pro + Ile159Ala
	Ala156Ser + Gly157Ser + Ile159Gln + Tyr161Glu
	Asn153Ser + Gly157Ser + Ile159Ala + Ser160Asp
	Gly155Gln + Ser158Asp + Ile159Gly + Tyr161Met
	Gly152Ser + Ser154Asp + Ala156Gln + Ile159Cys
50	Ala156His + Gly157Pro + Ser158Glu + Tyr161Met
	Ala156Pro + Gly157Asn + Ile159Met + Ser160Asp
	Ser154Glu + Gly155Asn + Ile159Met + Tyr161Ala

	Gly152Ser + Ala156His + Gly157Pro + Ile159Gly
	Asn153Ser + Ile159Leu + Ser160Glu + Tyr161Thr
	Gly152Asn + Ser154Asp + Ala156Ser + Gly157Asn
	Ser154Asp + Gly155Gln + Ile159Leu + Tyr161Thr
5	Asn153Ser + Ser154Asp + Gly155Asn + Ile159Met
	Gly152Asn + Asn153Gln + Gly155Asn + Ile159Val
	Asn153Glu + Ser154Glu + Gly157Asn + Ile159Leu
	Asn153Glu + Ser154Asp + Gly155Pro + Ala156Ser
	Ser154Asp + Gly155Asp + Ala156Gly + Gly157Asn
10	Gly152Ser + Gly157Asp + Ser158Asp + Ile159Ser
	Gly155Pro + Gly157Asp + Ser158Asp + Ile159Pro
	Ala156Glu + Gly157Glu + Ser158Glu + Tyr161Ile
	Asn153Glu + Ser154Asp + Gly155Asp + Ala156Pro
	Ser154Glu + Ala156Glu + Gly157Ser + Ile159Ser
15	Ala156Glu + Gly157Asn + Ser158Asp + Ile159Asn
	Gly152Asn + Asn153Asp + Gly155Glu + Tyr161Gln
	Gly152Pro + Asn153Asp + Gly155Glu + Gly157Gln
	Gly152Asp + Ala156Pro + Ile159Val + Ser160Asp
	Gly152Asp + Asn153Gln + Ile159Ala + Ser160Asp
20	Gly152Glu + Ser154Glu + Ile159Gln + Tyr161Cys
	Gly152Glu + Ser154Asp + Gly157Pro + Tyr161Leu
	Gly155Asp + Ala156Asp + Gly157Pro + Ser158Asp
	Gly155Glu + Ala156Asp + Gly157Gln + Ser158Asp
	Gly152Asp + Asn153Glu + Ile159Thr + Ser160Glu
25	Gly152Glu + Asn153Asp + Ile159Leu + Ser160Glu
	Ala156Thr + Ser158Asp + Ser160Glu + Tyr161Cys
	Ser158Glu + Ile159Met + Ser160Asp + Tyr161Pro
	Ser158Glu + Ile159Cys + Ser160Glu + Tyr161Gly
	Gly155Pro + Ser158Glu + Ile159Gln + Ser160Asp
30	Gly157Pro + Ser158Asp + Ser160Glu + Tyr161Met
	Gly152Glu + Ser154Glu + Gly157Asn + Ser160Glu
	Gly152Glu + Ser154Asp + Gly157Gln + Ser160Asp
	Gly152Glu + Ser154Asp + Gly157Ser + Ser160Glu
	Gly152Glu + Ala156Gly + Ser158Asp + Ser160Glu
35	Gly152Asp + Ser158Asp + Ile159Leu + Ser160Glu
	Gly152Asp + Gly155Gln + Ser158Asp + Ser160Glu
	Ala156Glu + Ser158Glu + Ser160Asp + Tyr161Gly
	Gly157Asp + Ser158Glu + Ile159His + Ser160Glu
	Gly152Asn + Ser154Glu + Gly155Asp + Ser158Asp
40	Asn153Glu + Ser154Asp + Gly157Pro + Ser160Glu
	Asn153Asp + Ser154Asp + Ile159Ser + Ser160Glu
	Asn153Asp + Ser154Asp + Ser160Asp + Tyr161Ile
	Gly152Asn + Ser154Glu + Gly157Glu + Ser158Asp
	Gly152Glu + Ala156Asp + Ser158Glu + Ile159Val
45	Asn153Asp + Ser154Glu + Ala156Ser + Gly157Asp
	Asn153Glu + Ser154Glu + Gly155Ser + Gly157Asp
	Ser154Glu + Gly155Asp + Gly157Pro + Ser160Asp
	Gly152Asp + Asn153Glu + Ser158Glu + Ile159Ala

40

	Ala181Asp
	Ala181Gln
	Ala181Glu
	Ala181Gly
5	Ala181His
	Ala181Pro
	Ala181Ser
	Ala181Thr
	Ser182Asp
10	Ser182Glu
	Phe183Ala
	Phe183Asn
	Phe183Asp
	Phe183Cys
15	Phe183Gln
	Phe183Glu
	Phe183Gly
	Phe183His
	Phe183Ile
20	Phe183Leu
	Phe183Met
	Phe183Pro
	Phe183Ser
	Phe183Thr
25	Phe183Tyr
	Phe183Val
	Ser184Asp
	Ser184Glu
	Gln185Asn
30	Gln185Asp
	Gln185Glu
	Gln185Ser

TABLE 20

35	Loop 5 - Double Mutation Variants
	Ala181Asp + Phe183Gln
	Ser182Asp + Gln185Asn
	Phe183Met + Gln185Glu
	Ser182Glu + Gln185Asn
40	Ala181Pro + Ser182Glu
	Ala181Asn + Gln185Glu
	Ser182Glu + Phe183Leu
	Ala181Pro + Gln185Asp
	Phe183Ser + Gln185Glu
45	Ala181Gln + Ser182Glu
	Phe183Ile + Gln185Glu
	Ala181Ser + Gln185Asp
	Ala181Gln + Phe183Ser
	Ala181Thr + Phe183Asn
50	Ala181Gly + Gln185Asp
	Ala181His + Ser182Glu
	Phe183Gln + Gln185Ser

	Phe183Pro + Gln185Ser
	Ala181Asn + Ser182Asp
	Ala181Ser + Gln185Glu
	Ala181Asn + Phe183Asn
5	Ala181His + Phe183Asp
	Ala181Asn + Ser182Glu
	Ser182Asp + Phe183His
	Ala181Asp + Phe183Ile
	Phe183Leu + Gln185Asp
10	Ser182Glu + Phe183Ser
	Ala181His + Gln185Asp
	Phe183Val + Gln185Asp
	Ser182Asp + Phe183Thr
	Phe183Gly + Gln185Asp
15	Ala181Thr + Gln185Glu
	Ala181His + Gln185Glu
	Ser182Asp + Phe183Val
	Ala181Asp + Phe183Ser
	Ser182Asp + Phe183Cys
20	Ala181Pro + Phe183Asp
	Ala181Gly + Phe183Ala
	Ala181Pro + Phe183Asn
	Phe183Pro + Gln185Asp
	Ser182Glu + Phe183Tyr
25	Phe183Cys + Gln185Ser
	Ala181Thr + Ser182Glu
	Ala181Pro + Phe183Ala
	Ser182Glu + Phe183Thr
	Ala181Pro + Phe183Pro
30	Ser182Glu + Gln185Ser
	Ala181Gln + Ser182Asp
	Phe183Gly + Gln185Glu
	Ala181Gln + Gln185Asp
	Phe183Ser + Gln185Asp
35	Ser182Asp + Phe183Met
	Phe183Ala + Gln185Asn
	Ala181Asp + Phe183His
	Phe183Val + Gln185Glu
	Ala181Ser + Ser182Glu
40	Ala181Asn + Phe183Pro
	Phe183Tyr + Gln185Glu
	Ala181Glu + Phe183Cys
	Ser182Glu + Phe183Ile

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TABLE 21

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Loop 5 - Triple Mutation Variants		
Ala181Glu +	Phe183Val +	Gln185Ser
Ala181Pro +	Ser182Asp +	Gln185Asn
Ala181Thr +	Phe183His +	Gln185Asp
Ser182Glu +	Phe183Ala +	Gln185Asn
Ala181Thr +	Ser182Asp +	Gln185Asn
Ala181Gln +	Ser182Asp +	Phe183Ala

	Ser182Asp + Phe183Asn + Gln185Asn
	Ala181Gln + Phe183Gln + Gln185Glu
	Ser182Asp + Phe183Met + Gln185Asn
	Ala181Pro + Ser182Glu + Phe183Gly
5	Ala181His + Phe183Ala + Gln185Ser
	Ala181Ser + Ser182Glu + Gln185Asn
	Ala181Gly + Phe183Ile + Gln185Glu
	Ala181Asn + Phe183Tyr + Gln185Asn
	Ser182Asp + Phe183Leu + Gln185Asn
10	Ser182Asp + Phe183Val + Gln185Asn
	Ala181Glu + Phe183Leu + Gln185Ser
	Ala181Glu + Phe183Tyr + Gln185Ser
	Ala181Gln + Ser182Asp + Phe183Gly
	Ala181Thr + Phe183Ile + Gln185Ser
15	Ala181Gln + Ser182Glu + Gln185Ser
	Ala181Gln + Ser182Glu + Phe183His
	Ala181Asp + Phe183Ala + Gln185Asn
	Ala181Thr + Ser182Asp + Phe183Thr
	Ala181Ser + Phe183Pro + Gln185Glu
20	Ser182Glu + Phe183Ala + Gln185Ser
	Ala181Asn + Phe183Cys + Gln185Ser
	Ala181Pro + Phe183Thr + Gln185Asp
	Ala181Thr + Phe183Val + Gln185Asn
	Ala181Gln + Ser182Asp + Gln185Ser
25	Ala181Asn + Ser182Asp + Gln185Ser
	Ser182Asp + Phe183Thr + Gln185Ser
	Ala181Ser + Phe183Asp + Gln185Asn
	Ser182Asp + Phe183Thr + Gln185Asn
	Ala181Gly + Phe183Asn + Gln185Ser
30	Ala181Asp + Phe183Met + Gln185Ser
	Ala181Asp + Phe183Pro + Gln185Asn
	Ala181Gly + Ser182Asp + Phe183Gly
	Ala181Gln + Ser182Glu + Gln185Asn
	Ala181Thr + Ser182Asp + Gln185Ser
35	Ala181Asn + Phe183Asn + Gln185Asp
	Ala181Thr + Phe183Asp + Gln185Ser
	Ala181Gln + Phe183Ser + Gln185Ser
	Ser182Asp + Phe183Gly + Gln185Ser
	Ala181Gly + Ser182Glu + Phe183Leu
40	Ala181Asn + Ser182Glu + Gln185Asn
	Ala181Glu + Ser182Glu + Phe183Ser
	Ala181Glu + Ser182Glu + Phe183Gly
	Ala181Glu + Ser182Glu + Phe183Leu
	Ala181Glu + Ser182Glu + Phe183Val
45	Ala181Glu + Ser182Asp + Phe183Met
	Ala181Asp + Ser182Asp + Phe183Met
	Ala181Asp + Ser182Asp + Phe183Cys
	Ala181Glu + Ser182Asp + Gln185Asn
	Ala181Asp + Ser182Asp + Gln185Asn
50	Ala181Glu + Ser182Glu + Phe183Asn
	Ala181Asp + Ser182Glu + Phe183Ser
	Ala181Glu + Ser182Asp + Gln185Ser
	Ala181Glu + Ser182Glu + Phe183Thr
	Ala181Glu + Ser182Asp + Phe183Leu

TABLE 22

Loop 5 - Quadruple Mutation Variants							
5	Ala181Ser	+	Ser182Asp	+	Phe183Ala	+	Gln185Ser
	Ala181Ser	+	Ser182Glu	+	Phe183Pro	+	Gln185Ser
	Ala181Gly	+	Ser182Asp	+	Phe183Gly	+	Gln185Asn
	Ala181Gly	+	Ser182Glu	+	Phe183Pro	+	Gln185Ser
	Ala181Thr	+	Ser182Glu	+	Phe183Thr	+	Gln185Ser
10	Ala181Gly	+	Ser182Glu	+	Phe183Thr	+	Gln185Ser
	Ala181His	+	Ser182Glu	+	Phe183His	+	Gln185Asn
	Ala181Gly	+	Ser182Glu	+	Phe183Ser	+	Gln185Ser
	Ala181Gln	+	Ser182Glu	+	Phe183His	+	Gln185Asn
	Ala181Asn	+	Ser182Glu	+	Phe183Cys	+	Gln185Ser
15	Ala181Pro	+	Ser182Glu	+	Phe183Met	+	Gln185Ser
	Ala181Gln	+	Ser182Asp	+	Phe183Gln	+	Gln185Asn
	Ala181Thr	+	Ser182Asp	+	Phe183His	+	Gln185Asn
	Ala181Gly	+	Ser182Glu	+	Phe183Leu	+	Gln185Ser
	Ala181Asn	+	Ser182Asp	+	Phe183Ile	+	Gln185Ser
20	Ala181Gly	+	Ser182Asp	+	Phe183Ala	+	Gln185Ser
	Ala181Asn	+	Ser182Asp	+	Phe183Ser	+	Gln185Asn
	Ala181Asn	+	Ser182Glu	+	Phe183Gly	+	Gln185Ser
	Ala181Asn	+	Ser182Glu	+	Phe183Met	+	Gln185Asn
	Ala181His	+	Ser182Glu	+	Phe183Asn	+	Gln185Asn
25	Ala181Gly	+	Ser182Glu	+	Phe183Tyr	+	Gln185Asn
	Ala181Asn	+	Ser182Asp	+	Phe183Asn	+	Gln185Asn
	Ala181Glu	+	Ser182Glu	+	Phe183Asn	+	Gln185Asn
	Ala181Asp	+	Ser182Glu	+	Phe183Ile	+	Gln185Asn
	Ala181Glu	+	Ser182Asp	+	Phe183Gln	+	Gln185Asn
30	Ala181Asp	+	Ser182Asp	+	Phe183His	+	Gln185Asn
	Ala181Glu	+	Ser182Asp	+	Phe183Ser	+	Gln185Asn
	Ala181Glu	+	Ser182Asp	+	Phe183Leu	+	Gln185Asn
	Ala181Glu	+	Ser182Asp	+	Phe183Leu	+	Gln185Ser
	Ala181Asp	+	Ser182Glu	+	Phe183Thr	+	Gln185Ser
35	Ala181Asp	+	Ser182Asp	+	Phe183Gln	+	Gln185Asn
	Ala181Asp	+	Ser182Asp	+	Phe183Ala	+	Gln185Asn
	Ala181Asp	+	Ser182Glu	+	Phe183Ala	+	Gln185Asn
	Ala181Glu	+	Ser182Asp	+	Phe183Met	+	Gln185Ser
	Ala181Glu	+	Ser182Glu	+	Phe183Thr	+	Gln185Asn
40	Ala181Asp	+	Ser182Asp	+	Phe183Gly	+	Gln185Ser
	Ala181Glu	+	Ser182Asp	+	Phe183Ala	+	Gln185Asn
	Ala181His	+	Ser182Glu	+	Phe183Glu	+	Gln185Asn
	Ala181Ser	+	Ser182Asp	+	Phe183Glu	+	Gln185Ser
	Ala181Ser	+	Ser182Asp	+	Phe183Asp	+	Gln185Ser
45	Ala181Pro	+	Ser182Glu	+	Phe183Asp	+	Gln185Ser
	Ala181Asp	+	Ser182Asp	+	Phe183Asp	+	Gln185Asn
	Ala181Glu	+	Ser182Asp	+	Phe183Glu	+	Gln185Ser
	Ala181Ser	+	Ser182Asp	+	Phe183Glu	+	Gln185Glu
	Ala181Gly	+	Ser182Glu	+	Phe183Glu	+	Gln185Glu
50	Ala181Gln	+	Ser182Glu	+	Phe183Asp	+	Gln185Asp
	Ala181Ser	+	Ser182Asp	+	Phe183Asp	+	Gln185Asp
	Ala181Thr	+	Ser182Asp	+	Phe183Asp	+	Gln185Asp
	Ala181Pro	+	Ser182Asp	+	Phe183Glu	+	Gln185Asp

	Ala181Asn + Ser182Glu + Phe183Asp + Gln185Asp
	Ala181Thr + Ser182Asp + Phe183Asp + Gln185Glu
	Ala181Pro + Ser182Glu + Phe183Glu + Gln185Glu
	Ala181Asn + Ser182Asp + Phe183Asp + Gln185Glu
5	Ala181Thr + Ser182Glu + Phe183Asp + Gln185Asp
	Ala181His + Ser182Glu + Phe183Glu + Gln185Glu
	Ala181Glu + Ser182Glu + Phe183Ser + Gln185Glu
	Ala181Glu + Ser182Glu + Phe183Val + Gln185Glu
	Ala181Asp + Ser182Glu + Phe183Pro + Gln185Glu
10	Ala181Glu + Ser182Glu + Phe183Thr + Gln185Asp
	Ala181Asp + Ser182Asp + Phe183Cys + Gln185Glu

TABLE 23

Loop 6 - Single Mutation Variants	
15	Val193Ala
	Val193Asn
	Val193Asp
	Val193Cys
	Val193Gln
20	Val193Glu
	Val193Gly
	Val193His
	Val193Met
	Val193Pro
25	Val193Ser
	Val193Thr
	Ala194Asn
	Ala194Asp
	Ala194Gln
30	Ala194Glu
	Ala194Gly
	Ala194His
	Ala194Pro
	Ala194Ser
35	Ala194Thr
	Pro195Asn
	Pro195Asp
	Pro195Gln
	Pro195Glu
40	Pro195Gly
	Pro195Ser
	Gly196Asn
	Gly196Asp
	Gly196Gln
45	Gly196Glu
	Gly196Pro
	Gly196Ser
	Val197Ala
	Val197Asp
50	Val197Cys
	Val197Gln
	Val197Glu

	Vall197Gly
	Vall197His
	Vall197Met
	Vall197Pro
5	Vall197Ser
	Vall199Ala
	Vall199Asn
	Vall199Asp
	Vall199Cys
10	Vall199Gln
	Vall199Glu
	Vall199Gly
	Vall199His
	Vall199Met
15	Vall199Pro
	Vall199Ser
	Vall199Thr
	Gln200Asn
	Gln200Ser
20	Ser201Asp
	Ser201Glu
	Thr202Asn
	Thr202Asp
	Thr202Gln
25	Thr202Glu
	Thr202Gly
	Thr202Pro
	Thr202Ser
	Tyr203Ala
30	Tyr203Asn
	Tyr203Asp
	Tyr203Gln
	Tyr203His
	Tyr203Ile
35	Tyr203Met
	Tyr203Pro
	Tyr203Ser
	Pro204Asn
	Pro204Asp
40	Pro204Gln
	Pro204Glu
	Pro204Gly
	Pro204Ser
	Gly205Asn
45	Gly205Asp
	Gly205Gln
	Gly205Glu
	Gly205Pro
	Gly205Ser
50	Ser206Asp
	Ser206Glu
	Thr207Asn
	Thr207Gln
	Thr207Glu

	Thr207Gly
	Thr207Pro
	Thr207Ser
	Tyr208Ala
5	Tyr208Asn
	Tyr208Asp
	Tyr208Cys
	Tyr208Gln
	Tyr208Glu
10	Tyr209Gly
	Tyr209His
	Tyr209Ile
	Tyr209Leu
	Tyr209Met
15	Tyr209Pro
	Tyr209Val
	Ala209Asn
	Ala209Asp
	Ala209Gln
20	Ala209Glu
	Ala209Gly
	Ala209His
	Ala209Pro
	Ala209Ser
25	Ala209Thr
	Ser210Asp
	Ser210Glu
	Leu211Ala
	Leu211Asn
30	Leu211Asp
	Leu211Cys
	Leu211Gln
	Leu211Gly
	Leu211His
35	Leu211Ile
	Leu211Met
	Leu211Pro
	Leu211Ser
	Leu211Thr
40	Leu211Val
	Asn212Glu
	Gly213Asn
	Gly213Asp
	Gly213Gln
45	Gly213Glu
	Gly213Pro
	Gly213Ser
	Thr214Asn
	Thr214Asp
50	Thr214Gln
	Thr214Glu
	Thr214Gly
	Thr214Pro
	Thr214Ser

TABLE 24

Loop 6 - Double Mutation Variants	
5	Gly196Asn + Ala209Asp
	Val199Ser + Tyr208Asn
	Pro195Asn + Thr207Asp
	Val197Ala + Asn212Asp
	Asn198Gln + Thr207Ser
10	Val199Gly + Tyr208Ile
	Gly196Asn + Ala209Pro
	Val199Gly + Gln200Ser
	Pro195Ser + Gly205Gln
	Val199Ser + Leu211Asp
15	Gly196Gln + Val197Asn
	Thr202Asn + Thr214Glu
	Ala194Thr + Thr202Pro
	Val199Asn + Ser210Glu
	Thr202Ser + Asn212Gln
20	Ser210Asp + Thr214Asn
	Pro195Gly + Asn212Asp
	Asn198Gln + Tyr208Gln
	Val197Asn + Thr214Glu
	Tyr208Asp + Leu211Gln
25	Thr202Ser + Ser210Glu
	Val197Cys + Ser210Glu
	Gln200Glu + Tyr203Gly
	Ala209Thr + Leu211Glu
	Val197Ser + Gln200Glu
30	Thr202Gly + Ser210Glu
	Gln200Ser + Gly213Pro
	Gly196Ser + Thr207Gly
	Pro204Gln + Ser210Glu
	Val199Cys + Pro204Gly
35	Gly213Pro + Thr214Pro
	Gly196Asn + Ser210Glu
	Thr207Gln + Ser210Glu
	Val199Met + Gln200Asp
	Thr202Ser + Tyr203Ile
40	Pro195Ser + Asn212Ser
	Val197Glu + Tyr208Gln
	Asn198Glu + Leu211Cys
	Gly196Gln + Ser206Glu
	Ala194Ser + Thr214Ser
45	Val197Ser + Tyr203Ala
	Ser210Asp + Gly213Pro
	Tyr203His + Gly213Asp
	Val197Ser + Val199Ser
	Ala209Pro + Ser210Asp
50	Thr207Asp + Thr214Ser
	Thr207Gly + Ala209His
	Pro195Asn + Asn198Asp
	Val197Pro + Ser206Asp

	Gln200Ser + Asn212Asp
	Val197Thr + Asn212Asp
	Gln200Asn + Thr214Glu
	Ala209Asp + Thr214Ser
5	Ala209Asn + Asn212Ser
	Ala194Ser + Asn212Glu
	Val197Glu + Gly213Asn
	Tyr203Cys + Asn212Asp
	Pro195Gln + Val197Cys
10	Asn198Ser + Tyr208Ala
	Gly205Gln + Ala209Glu
	Gly205Ser + Leu211Ser
	Gly205Gln + Tyr208Ala
	Ala194Ser + Asn198Asp
15	Ala194Thr + Pro195Ser
	Val199Thr + Pro204Glu
	Thr202Gln + Ser210Asp
	Ser206Glu + Leu211His
	Asn198Glu + Thr202Asn
20	Ser210Asp + Gly213Ser
	Gly196Ser + Thr202Gln
	Pro204Gln + Gly213Asp
	Asn198Glu + Pro204Gly
	Thr202Gly + Tyr208Met
25	Pro195Gly + Gly213Glu
	Pro195Ser + Pro204Asp
	Pro195Ser + Tyr203Thr
	Ala194Asn + Tyr203Pro
	Ala194Pro + Gln200Asp
30	Pro204Asp + Gly205Asn
	Gly196Pro + Asn198Gln
	Thr207Ser + Leu211Gly
	Pro195Ser + Leu211Ile
	Pro204Glu + Leu211Gly
35	Val199Ser + Tyr208Ala
	Gly196Ser + Ser210Asp
	Ala194Thr + Leu211Gly
	Thr207Ser + Ser210Glu
	Gly196Pro + Thr207Glu
40	Pro204Glu + Leu211Met
	Pro195Asn + Asn198Ser
	Tyr203Met + Thr207Gln
	Pro204Gly + Ala209Glu
	Val197Glu + Asn212Ser
45	Pro195Ser + Ala209Pro
	Gly196Ser + Leu211Gly
	Gly205Pro + Leu211Met
	Val197Gln + Pro204Ser
	Val199Asn + Ser206Asp
50	Val197Asp + Thr202Asn
	Gly196Gln + Thr214Gly
	Pro204Asn + Asn212Gln
	Val199Asn + Gln200Asn
	Pro195Gly + Leu211Gly

	Tyr203Cys + Pro204Ser
	Gln200Asp + Leu211Cys
	Asn198Gln + Ser210Glu
	Ala194Gly + Gln200Glu
5	Gly196Gln + Pro204Glu
	Val197Pro + Thr202Asn
	Ala194Gly + Val199Ala
	Ala194Thr + Leu211Asn
	Asn198Gln + Gly205Asp
10	Tyr203Asn + Leu211His
	Asn212Asp + Gly213Gln
	Asn198Gln + Ser206Asp
	Val199Thr + Gln200Glu
	Thr202Ser + Asn212Asp
15	Ala194Gly + Ser210Glu
	Ser206Glu + Ala209Asn
	Ala209Asp + Asn212Ser
	Val199Gly + Asn212Ser
	Ala194Pro + Gly213Asp
20	Gln200Asp + Pro204Gly
	Val197Thr + Tyr203Ala
	Asn198Gln + Leu211Pro
	Pro195Gln + Leu211Gln
	Gly196Gln + Thr214Glu
25	Pro195Asn + Ser210Glu
	Thr207Asn + Leu211Asp
	Ser210Glu + Gly213Pro
	Gly205Pro + Thr207Asp
	Gln200Glu + Thr202Gln
30	Thr202Ser + Gly213Asp
	Pro204Gln + Thr214Gln
	Gly196Ser + Gln200Asp
	Val197Ser + Gln200Asp
	Thr202Pro + Thr207Asp
35	Tyr203Thr + Tyr208His
	Pro195Gln + Thr202Asn
	Val197Asn + Asn212Asp
	Val197Met + Thr202Gln
	Val199Met + Thr202Pro
40	Ala209Glu + Leu211Met
	Gly196Asn + Val199His
	Ala194Gly + Ser206Glu
	Gly196Asn + Pro204Asn
	Gly196Asn + Gln200Glu
45	Val197Ser + Ser210Asp
	Pro195Gln + Pro204Gln
	Ala194His + Asn198Gln
	Val197Cys + Asn212Gln
	Asn198Glu + Ala209Ser
50	Ala194Gln + Val199Pro
	Asn198Asp + Val199Gln
	Asn198Asp + Thr214Pro
	Pro204Asn + Tyr208Asp
	Tyr203Ser + Tyr208Leu

	Gly196Gln + Ala209Asp
	Ser206Glu + Asn212Gln
	Thr207Ser + Ala209His
	Val197Thr + Ser210Asp
5	Tyr208Gln + Ser210Asp
	Asn198Ser + Ser210Glu
	Gly196Ser + Thr214Asp
	Ala194Gln + Thr202Asn
	Pro195Gly + Thr214Asn
10	Leu211Thr + Thr214Asp
	Pro195Ser + Asn198Glu
	Gly196Ser + Gly205Ser
	Ala194His + Thr202Asn
	Thr207Gly + Tyr208Met
15	Ala194Ser + Val197His

TABLE 25

Loop 6 - Triple Mutation Variants	
20	Ala194Thr + Ser206Glu + Tyr208Cys
	Gly196Asn + Tyr203Pro + Ala209Gly
	Pro195Gly + Asn198Ser + Thr207Glu
	Pro195Gly + Gly205Gln + Gly213Ser
	Tyr203Leu + Pro204Gln + Gly205Gln
	Gly196Gln + Val197Asn + Ser206Asp
25	Leu211Ser + Gly213Ser + Thr214Gln
	Pro195Asn + Pro204Glu + Gly205Gln
	Asn198Asp + Thr202Gly + Gly213Gln
	Tyr203Ala + Leu211His + Thr214Gln
	Ala194Thr + Val197Ser + Val199Gly
30	Ala194Gln + Thr207Asp + Thr214Ser
	Gly196Asn + Pro204Gln + Ala209Asn
	Thr202Pro + Tyr208Asp + Leu211Thr
	Val197Gly + Ala209Gln + Asn212Gln
	Gly196Ser + Gly205Asp + Leu211Ile
35	Ala194Ser + Val197Pro + Asn198Asp
	Gly196Asn + Asn198Gln + Leu211Ser
	Ala194Thr + Ala209His + Thr214Asp
	Ala194Pro + Pro195Ser + Asn212Asp
	Thr202Ser + Tyr203Gln + Ser210Asp
40	Thr202Ser + Tyr203Leu + Thr214Glu
	Ala194Ser + Pro195Gly + Leu211Val
	Ala194Pro + Thr207Glu + Leu211Ala
	Gly196Asn + Ser206Glu + Leu211Gly
	Gly196Ser + Gly205Ser + Ser210Asp
45	Ala194Thr + Val197Gly + Leu211Ser
	Pro204Glu + Ala209His + Thr214Pro
	Gly196Ser + Gly205Asp + Leu211His
	Val197Cys + Thr202Gly + Thr207Gln
	Asn198Ser + Pro204Gly + Gly213Asp
50	Ala194Gly + Ala209Pro + Ser210Asp
	Gly196Pro + Tyr203Val + Tyr208Cys
	Val199Ala + Thr207Asn + Tyr208Val

	Tyr203Cys + Ser210Asp + Leu211Pro
	Ala194Ser + Val197Ser + Gln200Asp
	Ala194Asn + Pro195Gly + Leu211Ile
5	Val199Ser + Leu211Asn + Gly213Asp
	Ala194Asn + Ser206Glu + Thr214Gly
	Ala194Gly + Pro195Gly + Val197Asp
	Pro195Gln + Ala209Ser + Ser210Asp
	Val197Thr + Asn198Gln + Tyr203Leu
	Val197Ala + Thr202Gln + Ser206Glu
10	Gly196Pro + Pro204Gly + Asn212Glu
	Thr202Gly + Pro204Glu + Tyr208Ser
	Gln200Ser + Thr202Pro + Pro204Ser
	Gln200Glu + Tyr203Thr + Pro204Asn
	Asn198Asp + Val199Gln + Pro204Asn
15	Ala194Pro + Pro195Gln + Val199Gly
	Pro195Asn + Pro204Asn + Ser206Glu
	Thr202Asn + Leu211Thr + Asn212Gln
	Gly196Gln + Thr202Pro + Gly213Asp
	Asn198Glu + Gln200Asn + Leu211Gly
20	Val199Gly + Thr202Gln + Gly213Glu
	Tyr203Ser + Thr207Pro + Ser210Asp
	Pro195Gly + Gly196Gln + Val197Glu
	Pro195Gly + Thr207Gly + Tyr208Ser
	Thr202Gly + Leu211Glu + Gly213Gln
25	Val197Gly + Thr202Pro + Asn212Glu
	Gly196Gln + Gly205Gln + Ser206Glu
	Pro195Gly + Val199Thr + Thr214Glu
	Gly196Ser + Gln200Ser + Leu211Asp
	Gly196Asn + Tyr208Glu + Thr214Pro
30	Tyr203Thr + Pro204Asn + Ser206Glu
	Val199Thr + Thr202Asn + Tyr208Gly
	Thr202Pro + Tyr203Thr + Pro204Glu
	Gly196Gln + Asn212Asp + Thr214Gln
	Pro195Gly + Thr202Gly + Asn212Ser
35	Pro195Gly + Tyr208Gln + Ser210Asp
	Ala194Pro + Ser206Glu + Leu211Ser
	Ala194His + Pro204Asn + Gly213Gln
	Gly196Ser + Tyr208Met + Ser210Asp
	Val197Glu + Val199Ser + Tyr203Asn
40	Thr202Gly + Ala209Asn + Asn212Asp
	Val197Ser + Ser210Asp + Gly213Pro
	Ala194Ser + Tyr208Ile + Asn212Glu
	Ala194Gly + Asn198Gln + Ala209His
	Ala194Ser + Thr207Pro + Gly213Glu
45	Val199Thr + Leu211Asp + Asn212Ser
	Val199Pro + Thr202Ser + Leu211Asn
	Ser206Glu + Tyr208Cys + Thr214Asn
	Ala209Ser + Leu211Ile + Asn212Glu
	Asn198Glu + Tyr208Ala + Ala209Ser
50	Ala194Pro + Asn198Asp + Gly213Gln
	Ala194Asn + Pro195Ser + Leu211Glu
	Gly196Pro + Pro204Gly + Gly205Pro
	Tyr203Ile + Tyr208Thr + Ala209Glu
	Gly196Gln + Thr202Gln + Asn212Asp

	Ala194Asn + Val197Pro + Thr202Pro
	Ala194Gln + Val199Gly + Ala209Asp
	Ala194Ser + Pro195Gly + Asn212Gln
	Pro195Gln + Tyr203Pro + Ser210Asp
5	Val197Thr + Thr202Gln + Tyr208Asn
	Ala194Thr + Gly196Ser + Leu211Asn
	Ala194Gly + Thr202Ser + Pro204Asp
	Ala194Gly + Gly205Glu + Gly213Ser
	Val199Pro + Thr207Pro + Tyr208Met
10	Ala194Pro + Asn198Glu + Ala209His
	Tyr208Leu + Ser210Glu + Thr214Pro
	Gly196Asn + Val199Ala + Gly205Asp
	Gly196Pro + Gly205Glu + Tyr208Ser
	Pro195Asn + Gly196Gln + Val197Cys
15	Asn198Ser + Gln200Glu + Leu211Asn
	Thr202Ser + Tyr203Cys + Thr214Gln
	Ala194Ser + Gly196Gln + Thr207Asp
	Gly196Ser + Gly205Glu + Tyr208Ile
	Tyr203Met + Gly205Asn + Gly213Pro
20	Pro204Gln + Gly205Asp + Ala209His
	Gly205Asn + Leu211Asp + Thr214Ser
	Tyr203Met + Ala209His + Leu211Met
	Val199Asn + Thr202Ser + Gly213Glu
	Val197Thr + Pro204Asp + Asn212Gln
25	Ala194Gly + Ser210Glu + Leu211Pro
	Val197His + Ala209Gly + Ser210Asp
	Gln200Glu + Thr202Gln + Tyr208His
	Ala194Ser + Ser206Asp + Leu211Ala
	Pro195Ser + Asn198Asp + Gly205Pro
30	Tyr203Pro + Thr207Asp + Thr214Pro
	Pro195Ser + Val199His + Leu211Pro
	Tyr203Met + Thr207Glu + Ala209His
	Val197Cys + Gln200Asn + Ser206Glu
	Val197Glu + Thr202Gln + Tyr208His
35	Pro195Gln + Val197Cys + Pro204Gly
	Val199Pro + Gly205Ser + Gly213Asp
	Ala194Thr + Thr207Ser + Ala209Glu
	Val197Met + Gly205Pro + Tyr208Gly
	Gly196Ser + Gly205Glu + Ala209Thr
40	Pro195Ser + Val199Thr + Gly205Ser
	Ala194Ser + Asn198Asp + Gly213Ser
	Asn198Glu + Val199Ser + Thr207Pro
	Ala194Thr + Gly196Pro + Ser210Glu
	Gly196Asn + Thr202Pro + Leu211Met
45	Tyr203Met + Asn212Asp + Thr214Ser
	Tyr203Gly + Ala209Ser + Ser210Asp
	Ala194Ser + Thr207Ser + Leu211Pro
	Tyr208Cys + Gly213Asn + Thr214Pro
	Val197Met + Pro204Glu + Gly213Ser
50	Gln200Ser + Tyr203Ala + Pro204Asp
	Pro195Gly + Ser206Asp + Leu211Ile
	Tyr203Gly + Tyr208Asp + Leu211Asn
	Val197Thr + Ser206Glu + Thr214Pro
	Tyr203Ala + Pro204Asn + Gly213Glu

	Tyr208Ile + Ala209Gly + Leu211Gln
	Asn198Ser + Pro204Gly + Asn212Glu
	Ala194Gln + Val197Cys + Pro204Asn
	Ala209Thr + Leu211Ser + Gly213Pro
5	Gly196Ser + Thr202Pro + Asn212Asp
	Val197His + Tyr203Gln + Tyr208Cys
	Val199Ser + Leu211Thr + Gly213Pro
	Pro195Asn + Val197Asn + Thr202Pro
	Val199Pro + Pro204Gly + Gly205Asn
10	Pro195Gly + Asn198Asp + Thr214Gly
	Gln200Glu + Tyr203Ser + Asn212Gln
	Pro195Gly + Val199Gln + Thr214Pro
	Thr202Ser + Pro204Ser + Gly213Glu
	Pro195Gly + Thr202Pro + Gly205Glu
15	Thr202Gln + Tyr203Gly + Ala209Asn
	Pro195Asn + Gly196Gln + Asn212Asp
	Thr202Gly + Tyr208Ile + Leu211Val
	Asn198Glu + Tyr203Cys + Pro204Gly
	Ala194Ser + Thr207Ser + Ser210Asp
20	Gln200Asp + Thr202Pro + Tyr203Ala
	Val199Cys + Ala209Gln + Ser210Asp
	Ala194Asn + Val199Cys + Leu211Pro
	Gln200Ser + Ser210Glu + Leu211Asn
	Tyr203Gln + Thr207Glu + Tyr208Ser
25	Ala194Thr + Thr202Asn + Thr207Gly
	Pro195Gly + Gly196Gln + Ser210Asp
	Gln200Ser + Pro204Gly + Ser206Glu
	Ala194Asn + Gly196Gln + Asn198Glu
	Val197Thr + Pro204Gln + Gly205Glu
30	Val199Ala + Gln200Asp + Gly213Asn
	Val197Met + Tyr203Val + Gly213Pro
	Ala194Gln + Tyr203Val + Thr214Glu
	Val199Cys + Ala209His + Leu211Met
	Thr202Gln + Tyr203Ile + Ala209Gln
35	Ala194Gly + Ser206Glu + Leu211Gly
	Gly196Pro + Tyr208Gly + Ser210Glu
	Val197Gln + Thr202Gly + Gly205Asp
	Val197Pro + Gly205Asp + Thr214Pro

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TABLE 26

Loop 6 - Quadruple Mutation Variants

	Pro195Asn + Val197Ala + Thr207Ser + Asn212Asp
	Asn198Gln + Val199Gly + Tyr208Ile + Asn212Asp
	Tyr203His + Leu211Pro + Asn212Gln + Gly213Gln
45	Ala194His + Asn198Ser + Thr202Asn + Ala209Asp
	Gly196Gln + Asn198Ser + Thr202Ser + Pro204Glu
	Pro195Gln + Asn198Gln + Gly205Glu + Ala209Pro
	Val199His + Pro204Asp + Gly205Pro + Leu211Gly
	Gly196Gln + Gly205Asn + Ser206Asp + Thr214Ser
50	Gln200Glu + Thr202Pro + Leu211Asn + Gly213Asn
	Gly196Gln + Pro204Asn + Asn212Gln + Thr214Gly
	Pro195Gly + Val199Asn + Gln200Asn + Leu211Gly

5 Pro195Gln + Pro204Ser + Gly205Glu + Tyr208Ile
 Val199Ala + Tyr203Gln + Thr207Gly + Ser210Glu
 Ala194His + Val199Ser + Pro204Asn + Gly205Glu
 Gly196Pro + Asn198Asp + Gln200Asn + Ala209Pro
 Pro195Gln + Gln200Asp + Tyr203Asn + Leu211Cys
 Pro195Ser + Thr202Pro + Asn212Asp + Thr214Ser
 Ala194Gly + Val197Glu + Tyr203Leu + Leu211Cys
 Asn198Gln + Thr202Pro + Tyr208Met + Thr214Glu
 Gly196Ser + Val199Ser + Gly205Gln + Ser210Glu
 10 Tyr203Ala + Gly205Gln + Ser206Asp + Leu211Gln
 Gly196Ser + Val199His + Gln200Asp + Thr207Ser
 Pro195Gln + Gly196Gln + Gln200Glu + Tyr203Ser
 Gly196Ser + Gln200Glu + Gly205Gln + Gly213Asn
 Pro195Ser + Gly196Asn + Ser206Glu + Thr214Gly
 15 Gly196Asn + Val199Asn + Ser206Glu + Tyr208Pro
 Val197Gln + Gly205Ser + Ser210Glu + Thr214Ser
 Pro195Asn + Gln200Glu + Gly205Asn + Leu211Pro
 Tyr203Pro + Tyr208His + Leu211Val + Thr214Pro
 Ala194His + Val199Ser + Thr202Gly + Tyr208Asp
 20 Pro195Asn + Val199Asn + Ser206Asp + Gly213Ser
 Ala194Ser + Pro195Asn + Val199Ala + Gly205Glu
 Ala194Thr + Gly196Gln + Val199Gly + Tyr203Ile
 Val199Ala + Ala209Asp + Leu211Val + Asn212Gln
 Val197Gly + Asn198Ser + Tyr203Leu + Ser210Asp
 25 Gln200Ser + Thr207Gly + Tyr208Thr + Ser210Asp
 Pro204Gly + Gly205Asp + Thr207Asn + Tyr208Leu
 Ala194Gln + Thr202Ser + Ala209Ser + Asn212Glu
 Val197Met + Thr202Gly + Pro204Gly + Thr214Glu
 Val199Ala + Pro204Gln + Gly205Asp + Tyr208Gly
 30 Asn198Glu + Tyr208Cys + Ala209Gln + Leu211Val
 Gln200Ser + Pro204Ser + Ala209Asn + Leu211Glu
 Pro195Ser + Val197Thr + Gly205Gln + Thr214Pro
 Pro195Asn + Thr202Asn + Gly205Asp + Tyr208Ser
 Pro195Gly + Tyr203Pro + Leu211Ala + Asn212Glu
 35 Thr202Gly + Pro204Asn + Gly205Asn + Gly213Gln
 Val197Gly + Gln200Glu + Tyr208Ala + Asn212Ser
 Ala194Ser + Pro195Ser + Tyr203Ala + Ala209Asp
 Pro195Gln + Val197Thr + Val199Pro + Ala209His
 Gly196Asn + Ser206Asp + Leu211His + Thr214Ser
 40 Val197Asp + Tyr203His + Tyr208Cys + Thr214Gly
 Ala194Gln + Pro195Asn + Ala209His + Ser210Asp
 Val199Ser + Gln200Ser + Tyr203Asn + Ser206Asp
 Ala194Asn + Pro195Gln + Ser206Glu + Gly213Ser
 Pro195Ser + Tyr203Met + Ser206Asp + Gly213Gln
 45 Ala194Gly + Val199Thr + Tyr208His + Gly213Pro
 Ala194Pro + Val197Cys + Gln200Asp + Pro204Gly
 Thr202Gln + Thr207Glu + Tyr208Cys + Leu211Pro
 Gly196Gln + Asn198Glu + Tyr203Gln + Gly205Pro
 Thr202Asn + Tyr203Pro + Gly205Ser + Gly213Glu
 50 Pro195Asn + Asn198Ser + Ala209Gly + Leu211Thr
 Asn198Asp + Gln200Ser + Tyr203Pro + Gly205Asn
 Pro195Gln + Val199Gly + Tyr203Asn + Thr207Glu
 Ala194Gln + Thr202Gln + Tyr203His + Tyr208His
 Ala194Ser + Pro204Asp + Thr207Pro + Tyr208Thr

	Asn198Gln + Val199Gln + Gln200Asn + Ala209Gln
	Ala194Gly + Asn198Ser + Pro204Asp + Ala209His
	Gly196Gln + Val197Thr + Ser206Glu + Ala209Pro
	Gln200Ser + Thr202Pro + Tyr203Thr + Thr207Gly
5	Ala194Thr + Val197Gly + Gln200Asn + Thr207Asp
	Val197Pro + Val199Asn + Gln200Glu + Leu211Ile
	Gly196Pro + Pro204Ser + Ala209Ser + Leu211Gln
	Pro195Gly + Gly196Gln + Asn198Gln + Tyr208Glu
	Gln200Ser + Tyr203Met + Gly205Glu + Tyr208Asn
10	Ala194Gln + Pro195Gly + Ala209Gly + Ser210Glu
	Gly196Asn + Val197Asn + Ser210Asp + Asn212Gln
	Gly196Gln + Thr202Ser + Gly205Ser + Ser210Glu
	Gln200Asn + Gly205Pro + Leu211Cys + Thr214Pro
	Ala194Ser + Gly196Gln + Thr207Ser + Ser210Asp
15	Val197Gln + Thr202Pro + Tyr203Ala + Ser206Asp
	Gly196Gln + Asn198Glu + Asn212Ser + Gly213Asn
	Pro195Asn + Val197Gln + Gly205Gln + Leu211Glu
	Thr207Glu + Tyr208Leu + Leu211Met + Gly213Gln
	Pro195Ser + Val197Pro + Pro204Glu + Leu211Cys
20	Pro195Gly + Gly196Ser + Val199Gln + Thr214Asp
	Val197Asn + Gly205Asn + Thr207Ser + Ser210Asp
	Ala194His + Tyr203His + Gly205Pro + Ser206Glu
	Pro195Asn + Asn198Gln + Val199Gln + Leu211Gln
	Val197Pro + Thr202Gly + Pro204Gly + Thr207Ser
25	Thr202Pro + Tyr203Leu + Leu211Ala + Thr214Asp
	Pro195Asn + Val199His + Tyr203Met + Thr207Glu
	Val199Cys + Pro204Gly + Thr207Ser + Thr214Asp
	Ala194Ser + Pro195Gln + Tyr203Thr + Tyr208Pro
	Val199Cys + Tyr203Cys + Ser206Asp + Tyr208Ala
30	Val197Thr + Thr202Gln + Leu211Glu + Asn212Ser
	Gly196Ser + Val199Pro + Ala209Gln + Leu211Asn
	Ala194Gly + Ala209Gln + Asn212Asp + Thr214Gln
	Ala194Gln + Thr207Asn + Ala209Pro + Leu211His
	Gly196Ser + Val197Ser + Thr202Gln + Leu211Gln
35	Ala194Thr + Val197Ser + Thr202Pro + Thr207Pro
	Gly196Pro + Thr202Pro + Gly205Glu + Gly213Pro
	Ala194Pro + Pro195Gly + Val197Asn + Val199Cys
	Thr202Gly + Thr207Ser + Tyr208Pro + Leu211Pro
	Thr202Asn + Pro204Asp + Thr207Ser + Gly213Asn
40	Gly196Gln + Val197Cys + Tyr203Met + Ala209Asn
	Gly196Gln + Ser206Glu + Thr207Ser + Gly213Pro
	Pro195Ser + Val199Cys + Ser210Glu + Asn212Ser
	Ala194Ser + Ser206Asp + Asn212Ser + Thr214Gln
	Gly196Gln + Gln200Ser + Thr202Gln + Ala209Ser
45	Gly196Gln + Tyr203Thr + Thr207Gln + Asn212Glu
	Ala194Pro + Thr202Gln + Tyr208Cys + Leu211Pro
	Gln200Asp + Tyr203Cys + Leu211Gln + Asn212Gln
	Gly196Asn + Tyr203Met + Leu211Asn + Gly213Asn
	Pro195Gln + Gly196Asn + Gln200Ser + Thr202Gln
50	Thr202Pro + Tyr203Gly + Asn212Ser + Thr214Gly
	Gln200Asp + Tyr203Thr + Pro204Gln + Gly205Ser
	Gly196Ser + Thr202Pro + Pro204Asn + Ala209Ser
	Gly196Ser + Gln200Ser + Pro204Gly + Ser210Asp
	Ala194Gln + Gln200Asn + Thr202Ser + Gly205Gln

5 Pro195Gly + Gln200Asn + Thr207Asp + Ala209His
 Gln200Asn + Thr202Ser + Tyr203Ala + Thr214Gly
 Gln200Glu + Ala209Pro + Leu211Ile + Gly213Asn
 Ala194Asn + Thr202Ser + Tyr203Met + Ser206Glu
 Val197Asn + Asn198Ser + Thr207Gln + Thr214Glu
 Val197Met + Gln200Ser + Pro204Glu + Ala209Pro
 Gly196Asn + Val199Asn + Leu211Glu + Asn212Gln
 Pro195Gln + Thr202Gln + Gly205Asp + Tyr208Asn
 Thr202Pro + Ser206Asp + Leu211Ile + Gly213Ser
 10 Gly196Ser + Gln200Glu + Thr202Gln + Tyr208Met
 Asn198Glu + Tyr203Thr + Tyr208Asn + Gly213Gln
 Asn198Ser + Ser210Glu + Leu211His + Thr214Pro
 Gly196Ser + Val197Gly + Pro204Glu + Thr214Ser
 Tyr203Met + Ser206Glu + Tyr208Ser + Ala209His
 15 Gly196Gln + Gln200Ser + Leu211Cys + Gly213Pro
 Ala194Gly + Val199Asn + Thr202Asn + Gly213Pro
 Asn198Ser + Thr202Asn + Tyr203Gly + Ser210Glu
 Val199Gln + Gln200Ser + Tyr203His + Thr214Asp
 Thr202Gln + Ser206Asp + Thr207Ser + Thr214Gly
 20 Ala194Thr + Tyr203Gln + Thr207Asp + Leu211Ile
 Ala209Ser + Ser210Asp + Asn212Gln + Gly213Ser
 Val197Ser + Tyr203Gly + Ser206Glu + Asn212Gln
 Ala194Ser + Asn198Ser + Gly205Gln + Ser210Asp
 Ala194Gln + Pro195Ser + Val197Gln + Pro204Asn
 25 Ala194Gly + Asn198Ser + Ala209Glu + Thr214Asn
 Val199Met + Ser206Asp + Gly213Asn + Thr214Ser
 Thr202Gln + Gly205Ser + Leu211Asp + Asn212Glu
 Pro195Ser + Ala209Gly + Gly213Asp + Thr214Asp
 Thr202Gln + Thr207Pro + Gly213Glu + Thr214Asp
 30 Ala194Ser + Thr207Pro + Ala209Glu + Ser210Glu
 Gln200Asn + Thr202Gln + Ala209Glu + Ser210Glu
 Gln200Ser + Ala209Asp + Ser210Asp + Asn212Gln
 Gly205Asn + Ala209Asp + Ser210Glu + Asn212Gln
 Pro204Gly + Leu211Gln + Asn212Glu + Gly213Asp
 35 Tyr203Gly + Pro204Asp + Gly205Glu + Leu211Ala
 Thr202Ser + Pro204Glu + Gly205Asp + Thr207Gln
 Thr202Gly + Pro204Asp + Gly205Glu + Gly213Asn
 Val199Gly + Ser210Asp + Leu211Asp + Asn212Gln
 Gly196Pro + Thr202Ser + Gly205Asp + Ser206Glu
 40 Val197Thr + Gly205Asp + Ser206Glu + Gly213Gln
 Pro204Asn + Gly205Glu + Ser206Glu + Asn212Ser
 Ala194His + Gly205Asp + Ser206Asp + Leu211His
 Pro195Asn + Ser206Glu + Thr207Asp + Asn212Ser
 Tyr203Met + Ser206Glu + Thr207Glu + Leu211Gly
 45 Gly196Gln + Pro204Asn + Ser206Asp + Thr207Glu
 Ala194Thr + Val197Cys + Ser206Asp + Thr207Asp
 Ala194Pro + Tyr208Asp + Ala209Asp + Gly213Gln
 Gln200Asp + Tyr208Thr + Ala209Ser + Ser210Glu
 Val199Asn + Gln200Asp + Thr202Gln + Ser210Asp
 50 Ala194Ser + Gln200Glu + Thr202Gly + Ser210Glu
 Val199Cys + Gln200Asp + Ala209Gln + Ser210Asp
 Ala194Gln + Val197Asp + Tyr208Gln + Asn212Asp
 Pro195Gly + Asn198Glu + Ser210Asp + Leu211Gln
 Ala194Pro + Pro195Asn + Asn198Asp + Ser210Asp

Pro195Gln + Asn198Glu + Val199Ser + Ser210Asp
 Val197His + Asn198Glu + Thr207Pro + Ser210Asp
 Gly196Pro + Val197Gly + Asn198Asp + Ser210Glu
 Asn198Glu + Ala209Gln + Leu211Glu + Thr214Pro
 5 Gln200Glu + Tyr203Asn + Thr207Gln + Ala209Glu
 Pro195Ser + Gly196Ser + Gln200Glu + Ala209Asp
 Pro195Ser + Gln200Asp + Ala209Glu + Leu211Ala

TABLE 27

Loop 6 - Quintuple Mutation Variants	
10	Val197Ala + Asn198Gln + Thr207Ser + Tyr208Ile + Asn212Asp
	Ala194Gly + Gly196Ser + Val197Gly + Gln200Glu + Leu211Gly
	Gln200Asp + Thr202Ser + Tyr203Ser + Pro204Ser + Asn212Ser
	Pro195Ser + Val199Ala + Gly205Asn + Ser206Glu + Gly213Ser
15	Val199His + Pro204Asp + Gly205Pro + Leu211Gly + Thr214Ser
	Ala194Gly + Thr207Pro + Ser210Glu + Leu211Cys + Gly213Gln
	Pro195Asn + Gly196Pro + Asn198Ser + Thr202Gly + Gly213Asn
	Gly196Ser + Val197Gln + Pro204Ser + Gly205Asp + Leu211Gly
	Pro195Ser + Gly196Gln + Pro204Asn + Gly213Asp + Thr214Gly
20	Pro195Gly + Val199Asn + Gln200Asn + Ser210Glu + Leu211Gly
	Val197Ser + Val199Gly + Tyr203Thr + Gly205Ser + Asn212Glu
	Pro195Asn + Asn198Asp + Thr202Ser + Ala209His + Asn212Gln
	Gly196Asn + Gly205Pro + Thr207Pro + Asn212Asp + Gly213Gln
	Val197Gly + Asn198Asp + Val199His + Gly205Gln + Tyr208His
25	Tyr203Val + Thr207Gly + Ala209Ser + Asn212Glu + Gly213Gln
	Ala194Thr + Pro195Gly + Gly196Ser + Tyr203Asn + Asn212Ser
	Pro195Gln + Thr202Gly + Tyr203Leu + Pro204Gly + Ser210Asp
	Pro195Asn + Val199Ala + Thr202Asn + Tyr208Pro + Ser210Asp
	Ala194Pro + Pro195Gly + Asn198Glu + Pro204Asn + Tyr208Pro
30	Ala194Ser + Val197Thr + Asn198Ser + Thr202Pro + Asn212Ser
	Gly196Ser + Val199Pro + Thr207Ser + Tyr208Thr + Asn212Gln
	Gly205Glu + Tyr208Gly + Leu211Ile + Asn212Ser + Thr214Gly
	Gln200Ser + Thr202Gly + Thr207Asp + Leu211Ser + Thr214Gln
	Pro195Asn + Thr207Asp + Tyr208Asn + Asn212Ser + Gly213Asn
35	Pro195Asn + Tyr203Ser + Pro204Glu + Leu211Val + Asn212Gln
	Gln200Asp + Gly205Ser + Tyr208Met + Leu211Asn + Asn212Ser
	Ala194Ser + Val199Pro + Gly205Glu + Tyr208Met + Gly213Ser
	Asn198Ser + Gln200Glu + Thr202Gly + Ala209Gln + Leu211Asn
	Gly196Pro + Asn198Glu + Thr202Ser + Ala209Thr + Thr214Gly
40	Ala194Gln + Pro195Gly + Gly196Asn + Tyr203Ile + Thr214Pro
	Pro195Gln + Val197Cys + Thr202Gln + Tyr203Cys + Tyr208His
	Val199Pro + Pro204Gly + Gly205Ser + Thr207Ser + Gly213Asp
	Tyr203Gly + Pro204Ser + Gly205Asn + Ala209Thr + Ser210Asp
	Ala194Ser + Thr207Ser + Tyr208Cys + Leu211Pro + Thr214Pro
45	Pro195Gly + Val199His + Gly205Glu + Ala209Asn + Leu211Pro
	Pro204Asn + Tyr208Ile + Ala209Gly + Leu211Gln + Gly213Glu
	Ala194Gln + Val197Cys + Asn198Ser + Pro204Gly + Asn212Glu
	Asn198Glu + Pro204Asn + Ala209Thr + Leu211Ser + Gly213Pro
	Gly196Ser + Val199Ser + Pro204Asp + Thr207Gly + Tyr208Ile
50	Gln200Glu + Thr202Ser + Tyr203Ala + Pro204Gly + Tyr208Met
	Asn198Gln + Thr202Pro + Gly205Asn + Thr207Glu + Thr214Pro
	Gly196Ser + Val199Pro + Ala209Gln + Ser210Asp + Leu211Asn

Ala194Gly + Thr207Asn + Ala209Gln + Asn212Asp + Thr214Gln
 Pro195Gly + Asn198Gln + Val199Thr + Tyr208His + Leu211Ile
 Ala194Pro + Thr202Gly + Thr207Ser + Tyr208Pro + Leu211Pro
 Gly196Ser + Val197Ala + Gln200Asn + Thr202Pro + Ser210Glu
 5 Val197Gln + Thr202Asn + Tyr203Asn + Gly205Asp + Tyr208Ala
 Gly196Pro + Tyr203Ile + Pro204Asn + Leu211Ala + Thr214Gln
 Ala194Asn + Gln200Asn + Pro204Gln + Ala209Thr + Gly213Ser
 Ala194His + Pro195Gly + Gln200Ser + Leu211Asn + Asn212Ser
 Ala194Ser + Gly196Ser + Gln200Asn + Ser206Asp + Thr207Gly
 10 Gly196Asn + Tyr203Asn + Tyr208Ala + Ala209Pro + Gly213Gln
 Ala194Thr + Val199Asn + Tyr203Ser + Tyr208His + Asn212Asp
 Val197Glu + Val199Ala + Tyr208Gln + Ala209Gly + Leu211Val
 Gln200Asn + Thr202Ser + Tyr203Ala + Thr207Gln + Thr214Gly
 Val197Asn + Asn198Ser + Thr202Pro + Thr207Gln + Thr214Glu
 15 Pro195Gln + Asn198Glu + Gln200Ser + Tyr203Cys + Gly213Gln
 Gly196Gln + Asn198Ser + Thr202Asn + Tyr203Ser + Gly205Pro
 Ala194Thr + Thr207Pro + Tyr208Ile + Ala209Pro + Thr214Asn
 Asn198Ser + Val199Pro + Thr202Asn + Tyr203Gly + Asn212Glu
 Ala194Asn + Thr202Asn + Ser210Asp + Leu211Val + Asn212Ser
 20 Val197Ser + Val199His + Thr202Asn + Ser210Asp + Leu211Cys
 Gly196Pro + Val197Cys + Val199Met + Tyr203Ser + Leu211Asn
 Ala194Gly + Gly196Pro + Val199His + Thr202Pro + Ser210Glu
 Gly196Ser + Val197His + Asn198Glu + Thr202Pro + Asn212Ser
 Ala194His + Gly196Asn + Val197Gln + Thr202Ser + Gly205Glu
 25 Pro195Gly + Gly196Pro + Asn198Ser + Gln200Ser + Thr202Pro
 Val197Asn + Asn198Asp + Gln200Asn + Thr202Gln + Tyr208Ala
 Pro195Asn + Thr202Ser + Pro204Asp + Tyr208Ala + Ala209Ser
 Tyr203His + Pro204Asn + Gly205Asp + Thr207Gln + Leu211Gly
 Ala194Asn + Pro195Gln + Gly196Gln + Pro204Asn + Gly213Glu
 30 Val197Thr + Val199His + Ser206Glu + Gly213Asn + Thr214Asn
 Gly196Gln + Val197Asn + Tyr203Thr + Pro204Ser + Thr214Asp
 Gly196Asn + Val199Gly + Gln200Ser + Tyr203Asn + Gly213Glu
 Ala194Thr + Gln200Asn + Thr202Ser + Gly205Gln + Gly213Asp
 Pro195Ser + Asn198Ser + Val199Gly + Tyr203Val + Thr207Glu
 35 Ala194Asn + Pro195Gly + Thr202Gly + Tyr203Gly + Leu211Asp
 Pro195Ser + Val197Ser + Tyr203Cys + Gly205Glu + Ala209Thr
 Gly196Gln + Val197Gly + Gly205Ser + Tyr208Leu + Thr214Asp
 Ala194Gln + Gly196Asn + Tyr203Pro + Pro204Ser + Gly213Asp
 Gly196Gln + Thr202Gly + Tyr203Cys + Pro204Gln + Ser206Glu
 40 Val197Pro + Val199Met + Tyr203Val + Pro204Gly + Thr214Asp
 Gly196Pro + Gln200Asn + Tyr203Cys + Ala209Thr + Thr214Asn
 Asn198Gln + Pro204Asn + Thr207Gln + Gly213Pro + Thr214Asp
 Pro195Gly + Val197Ser + Val199Ala + Thr207Asp + Leu211Gly
 Pro195Gln + Asn198Gln + Ser206Asp + Thr207Ser + Ala209Ser
 45 Ala194Ser + Tyr203Leu + Ala209Asn + Ser210Asp + Thr214Ser
 Val199His + Thr202Ser + Gly205Asn + Leu211Pro + Asn212Gln
 Gly196Ser + Asn198Ser + Thr207Asn + Tyr208Gln + Ser210Glu
 Pro195Asn + Asn198Gln + Thr207Ser + Gly213Asn + Thr214Gly
 Gly196Gln + Gln200Ser + Pro204Asn + Gly205Gln + Gly213Asp
 50 Pro204Asn + Ser206Glu + Tyr208Leu + Ala209Gly + Asn212Gln
 Val197Thr + Val199Gly + Gln200Asp + Thr202Pro + Thr207Gly
 Pro195Gln + Val199Ser + Thr202Asn + Gly205Asp + Ala209Gln
 Gly196Gln + Tyr203Thr + Tyr208Cys + Leu211Ala + Thr214Glu
 Asn198Gln + Gln200Ser + Pro204Gln + Asn212Ser + Gly213Pro

Vall197Pro + Vall199Asn + Thr202Gln + Tyr203Asn + Gly213Ser
 Ala194Ser + Gln200Ser + Thr202Gln + Thr207Gln + Ala209Glu
 Thr202Gly + Tyr203Thr + Tyr208Pro + Gly213Asp + Thr214Glu
 Vall197Gln + Pro204Gly + Gly205Ser + Ala209Glu + Ser210Asp
 5 Ala194Ser + Vall199Ala + Tyr208Ala + Ala209Glu + Ser210Glu
 Vall199Ala + Gln200Ser + Gly205Pro + Asn212Glu + Gly213Asp
 Ala194Pro + Thr202Ser + Pro204Glu + Gly205Asp + Ala209Pro
 Pro204Glu + Gly205Glu + Thr207Gly + Tyr208Ser + Leu211Ile
 Pro195Gln + Vall197Thr + Pro204Glu + Gly205Asp + Leu211Val
 10 Vall199His + Gly205Asp + Ser206Glu + Ala209Gln + Asn212Gln
 Tyr203Ala + Gly205Glu + Ser206Asp + Tyr208Ile + Asn212Gln
 Pro195Asn + Gly205Glu + Ser206Asp + Tyr208Ser + Ala209Ser
 Vall197His + Pro204Gly + Gly205Glu + Ser206Asp + Tyr208Cys
 Thr202Asn + Pro204Ser + Gly205Asp + Ser206Asp + Tyr208Thr
 15 Ala194Asn + Thr202Ser + Tyr203Gly + Ser206Glu + Thr207Glu
 Pro195Ser + Gly196Gln + Vall199Thr + Ser206Glu + Thr207Asp
 Gly196Pro + Ser206Asp + Thr207Glu + Tyr208Thr + Leu211His
 Ala194His + Gly196Gln + Pro204Asn + Tyr208Asp + Ala209Asp
 Vall199Ala + Tyr203Pro + Tyr208Asp + Ala209Asp + Asn212Gln
 20 Vall199Ala + Thr202Ser + Thr207Glu + Tyr208Asp + Thr214Ser
 Gly196Asn + Thr202Gln + Pro204Ser + Thr207Asp + Tyr208Asp
 Pro195Gln + Gln200Glu + Thr202Pro + Tyr203Pro + Ser210Asp
 Gly196Pro + Vall197Thr + Asn198Gln + Gln200Asp + Ser210Asp
 Gly196Gln + Asn198Glu + Thr207Pro + Tyr208Ser + Ser210Glu
 25 Ala194Pro + Asn198Glu + Thr207Pro + Ala209His + Ser210Glu
 Asn198Glu + Vall199Gln + Pro204Ser + Tyr208Asn + Ser210Asp
 Pro195Gly + Asn198Glu + Thr207Gly + Tyr208Cys + Ser210Asp
 Asn198Asp + Vall199Thr + Leu211Asp + Asn212Ser + Thr214Gly
 Gly196Pro + Asn198Gln + Gln200Glu + Tyr203Asn + Ala209Glu
 30 Gly196Pro + Tyr203Thr + Pro204Asp + Ser206Asp + Ala209Gln
 Pro195Asn + Gly196Pro + Asn198Asp + Ala209Pro + Asn212Glu
 Pro195Asn + Gly196Gln + Gly205Asp + Thr207Glu + Leu211Thr
 Thr202Asn + Pro204Asp + Thr207Asp + Tyr208Met + Thr214Pro
 Tyr203Gly + Pro204Asp + Thr207Asp + Asn212Gln + Thr214Gly
 35 Pro195Ser + Tyr203His + Pro204Glu + Thr207Asp + Gly213Gln
 Asn198Glu + Gln200Glu + Tyr203Cys + Pro204Gly + Asn212Gln
 Vall197Glu + Vall199Gly + Thr202Gly + Tyr203Ser + Gly213Glu
 Pro204Gly + Thr207Asn + Ala209His + Ser210Asp + Asn212Asp
 Pro195Gly + Gly196Gln + Thr202Gln + Ser210Asp + Asn212Asp
 40 Thr202Asn + Tyr203Asn + Gly205Pro + Ser210Asp + Asn212Asp
 Thr202Gln + Tyr203Gln + Ser210Asp + Asn212Asp + Gly213Gln
 Gly196Ser + Ser210Asp + Leu211Gly + Asn212Asp + Thr214Gln
 Gly196Pro + Ala209Ser + Ser210Glu + Leu211Asn + Asn212Asp
 Gly205Ser + Ala209Pro + Ser210Glu + Asn212Asp + Thr214Pro
 45 Pro195Gly + Tyr203Gly + Ser210Asp + Asn212Asp + Thr214Ser
 Pro195Gln + Vall197Asn + Vall199Cys + Tyr208Glu + Ser210Asp
 Vall197Ser + Tyr203Gly + Pro204Glu + Thr207Ser + Tyr208Asp
 Pro195Ser + Gly196Asn + Vall197Asp + Vall199Gly + Ser210Glu
 Gly196Pro + Vall197Asp + Thr202Pro + Ser210Glu + Thr214Pro
 50 Vall197Glu + Vall199His + Tyr208Thr + Leu211Gln + Thr214Glu
 Asn198Asp + Vall199Asn + Thr207Asn + Ala209His + Gly213Asp
 Vall197His + Asn198Glu + Tyr203Gln + Tyr208Cys + Gly213Asp
 Pro195Asn + Vall197Asn + Asn198Glu + Thr202Pro + Gly213Asp
 Pro195Ser + Asn198Glu + Tyr203Ser + Gly205Ser + Ala209Asp

	Pro195Gly + Gly196Asn + Asn198Asp + Val199Met + Ala209Glu
	Pro195Gln + Asn198Glu + Thr202Asn + Pro204Gly + Ala209Asp
	Val197Glu + Gln200Glu + Thr202Gly + Tyr208Ala + Gly213Gln
	Val197Asp + Gln200Asp + Thr207Ser + Tyr208Ile + Ala209Ser
5	Val197Asp + Gln200Glu + Ala209Ser + Leu211Gly + Asn212Ser
	Val197Glu + Gln200Asp + Thr202Asn + Gly205Gln + Asn212Gln
	Ala194Pro + Gly196Pro + Val197Met + Gln200Glu + Asn212Asp
	Gly196Gln + Gln200Glu + Thr202Pro + Tyr203Ile + Asn212Glu
	Ala194His + Gln200Asp + Asn212Glu + Gly213Pro + Thr214Asn
10	Val199Pro + Gln200Glu + Pro204Gly + Asn212Glu + Gly213Ser
	Asn198Ser + Gln200Asp + Gly205Pro + Thr207Ser + Asn212Glu
	Ala194Asn + Gln200Asp + Gly205Asn + Tyr208Asn + Asn212Asp
	Pro195Asn + Gln200Ser + Thr202Pro + Pro204Asp + Ala209Glu
	Pro195Ser + Thr202Asn + Tyr203Cys + Pro204Glu + Ala209Asp
15	Ala194His + Asn198Ser + Thr202Asn + Pro204Glu + Ala209Asp
	Ala194His + Pro204Asn + Ser206Glu + Ala209Glu + Thr214Ser
	Pro195Gly + Val197Cys + Ser206Glu + Ala209Glu + Asn212Ser
	Thr202Gly + Ser206Glu + Thr207Ser + Tyr208Met + Ala209Glu
	Ala194Gly + Gln200Glu + Thr207Asp + Leu211Ser + Thr214Pro
20	Pro195Asn + Val199Ser + Gln200Glu + Gly205Asn + Thr207Asp
	Ala194Gln + Asn198Gln + Gly205Pro + Ser210Asp + Gly213Asp
	Gly196Ser + Thr207Gly + Ser210Glu + Leu211Thr + Gly213Asp
	Asn198Gln + Pro204Gln + Thr207Asp + Tyr208Thr + Ser210Glu
	Ala194Ser + Gly196Gln + Thr207Glu + Ser210Glu + Leu211Thr
25	Thr207Glu + Ser210Glu + Asn212Ser + Gly213Ser + Thr214Ser
	Val197Cys + Thr207Glu + Ala209His + Ser210Glu + Asn212Ser
	Asn198Glu + Val199Met + Tyr208Ala + Gly213Gln + Thr214Asp
	Ala194Gln + Asn198Glu + Ala209Pro + Leu211His + Thr214Asp
	Asn198Asp + Thr207Pro + Leu211Gly + Asn212Ser + Thr214Asp
30	Ala194Ser + Gly196Asn + Asn198Asp + Pro204Gln + Thr214Glu

TABLE 28

Loop 6 - Sextuple Mutation Variants	
35	Ala194Gln + Val197Ser + Thr202Ser + Tyr203Ser + Ala209Ser + Asn212Asp
	Pro195Ser + Val199Cys + Gly205Ser + Leu211Thr + Asn212Glu + Gly213Pro
	Val197Thr + Asn196Ser + Val199Pro + Gln200Ser + Thr202Ser + Leu211Asn
40	Thr202Gly + Pro204Ser + Gly205Asn + Tyr208Asp + Gly213Gln + Thr214Pro
	Val197Gly + Gln200Glu + Thr202Gly + Tyr208Ala + Leu211Val + Asn212Ser
	Ala194Pro + Gly196Ser + Val199Cys + Tyr203Ala + Pro204Ser + Ala209Asp
45	Pro195Asn + Val199Pro + Thr202Asn + Tyr203Gly + Thr207Asp + Gly213Asn
	Ala194Gln + Thr202Ser + Tyr203Ile + Pro204Asn + Gly205Asp + Tyr208Ser
50	Ala194Gln + Val197His + Ala209Ser + Ser210Asp + Leu211Gly + Asn212Gln
	Thr202Gly + Gly205Pro + Ser210Asp + Leu211Ala + Gly213Ser

+ Thr214Gln
 Ala194His + Gln200Ser + Thr202Gly + Pro204Ser + Tyr208His
 + Gly213Glu
 Ala194Asn + Pro195Gln + Gly205Asn + Tyr208Ser + Leu211Val
 5 + Thr214Pro
 Gly196Pro + Asn198Ser + Gln200Ser + Thr202Asn + Tyr208Ile
 + Thr214Glu
 Pro195Asn + Gly205Pro + Thr207Gln + Ser210Glu + Leu211Asn
 + Gly213Pro
 10 Ala194Ser + Val197Gly + Asn198Asp + Tyr203Cys + Gly205Gln
 + Leu211Met
 Ala194Ser + Val197Asp + Val199Gln + Tyr203Cys + Gly205Ser
 + Gly213Gln
 Ala194Pro + Thr202Gly + Thr207Ser + Tyr208Met + Leu211Pro
 15 + Gly213Glu
 Ala194Thr + Pro195Asn + Gly196Gln + Gln200Ser + Thr202Asn
 + Pro204Glu
 Ala194Gln + Gly196Asn + Val197Ser + Asn198Ser + Val199Thr
 + Ser210Glu
 20 Gly196Ser + Val199Gly + Tyr203Ile + Pro204Asn + Leu211Asp
 + Thr214Gln
 Ala194Asn + Gln200Asn + Pro204Gln + Ala209Thr + Leu211Asn
 + Gly213Ser
 Ala194His + Pro195Gly + Gly196Asn + Gln200Ser + Tyr203Ser
 25 + Asn212Ser
 Ala194Pro + Val197Met + Val199Asn + Thr202Ser + Ser206Asp
 + Thr207Asn
 Pro195Gln + Thr202Pro + Gly205Asn + Ala209Pro + Asn212Ser
 + Thr214Asn
 30 Pro195Asn + Asn196Glu + Val199His + Pro204Asn + Thr207Gly
 + Leu211Met
 Gly196Ser + Pro204Asn + Thr207Pro + Asn212Asp + Gly213Ser
 + Thr214Pro
 Ala194Ser + Pro195Ser + Val197Cys + Pro204Asn + Thr207Glu
 35 + Gly213Gln
 Ala194His + Pro195Gly + Val197Gly + Val199Gln + Thr207Gly
 + Asn212Glu
 Ala194Gln + Pro195Ser + Val197Ser + Tyr203Met + Leu211Glu
 + Gly213Asn
 40 Ala194Asn + Gly196Asn + Pro204Asp + Thr207Pro + Tyr208Ser
 + Thr214Ser
 Pro195Asn + Thr202Gly + Gly205Asp + Thr207Gln + Tyr208Thr
 + Ala209Asn
 Ala194His + Pro195Gly + Val197His + Gly205Gln + Ala209Glu
 45 + Thr214Asn
 Ala194Gln + Asn198Gln + Tyr203Met + Ala209Gln + Ser210Glu
 + Leu211Gly
 Ala194Pro + Gly196Ser + Gln200Ser + Thr202Pro + Thr207Asp
 + Ala209Gly
 50 Pro195Gln + Gly196Ser + Asn198Gln + Gly205Ser + Ser210Asp
 + Leu211Val
 Asn198Gln + Val199Met + Gln200Glu + Thr202Gly + Gly205Asn
 + Tyr208Ala
 Ala194Pro + Val199Ala + Pro204Asn + Thr207Gln + Leu211Glu

+ Gly213Ser
 Gly196Pro + Val197Thr + Val199His + Gly205Asn + Ser206Asp
 + Thr207Asn
 Pro195Asn + Gly196Ser + Thr202Asn + Tyr203Gly + Leu211Asn
 5 + Asn212Glu
 Ala194Ser + Pro195Gln + Val197Cys + Ser206Glu + Tyr208His
 + Asn212Gln
 Pro195Gln + Gly196Pro + Val197Thr + Ser210Asp + Gly213Ser
 + Thr214Pro
 10 Ala194Gly + Pro195Ser + Thr202Gly + Pro204Glu + Tyr208Thr
 + Gly213Pro
 Ala194Asn + Pro195Asn + Gly196Asn + Gly205Pro + Ala209Asn
 + Ser210Asp
 Pro195Ser + Val199Gln + Tyr208Asn + Ala209Gln + Leu211Gly
 15 + Gly213Gln
 Asn198Asp + Val199Ala + Thr202Asn + Ala209Pro + Asn212Gln
 + Thr214Gly
 Pro195Asn + Gly196Gln + Val199Pro + Ser206Glu + Tyr208Ala
 + Leu211Val
 20 Ala194Gln + Pro195Ser + Asn198Asp + Val199Ser + Thr202Pro
 + Ala209Gln
 Pro195Gly + Val199Met + Gly205Glu + Thr207Asn + Ala209Pro
 + Gly213Pro
 Pro195Asn + Gly196Gln + Gln200Asp + Thr207Asn + Ala209Gly
 25 + Asn212Ser
 Gly196Gln + Val197His + Thr207Asn + Ser210Asp + Leu211Ala
 + Gly213Gln
 Ala194Gly + Val197Thr + Tyr203Met + Gly205Glu + Ala209Gly
 + Thr214Gly
 30 Gln200Glu + Thr202Asn + Tyr203Gly + Thr207Asn + Asn212Gln
 + Gly213Pro
 Gly196Asn + Thr202Ser + Pro204Glu + Leu211Pro + Gly213Ser
 + Thr214Asn
 Pro195Gly + Val197Asn + Val199Gln + Gln200Asn + Thr207Gly
 35 + Asn212Ser
 Pro195Gln + Gly196Pro + Val197His + Tyr203Gly + Ser206Asp
 + Thr214Ser
 Gly196Gln + Tyr203His + Thr207Asn + Leu211Asn + Gly213Pro
 + Thr214Asp
 40 Ala194Asn + Asn198Ser + Gln200Asn + Thr202Ser + Tyr203Ile
 + Ala209Thr
 Ala194His + Val197Cys + Gln200Ser + Tyr203Gly + Thr207Gly
 + Ala209His
 Asn198Gln + Val199Thr + Gln200Asp + Pro204Asn + Asn212Ser
 45 + Gly213Gln
 Gly196Pro + Tyr203Gln + Pro204Ser + Thr207Asn + Tyr208Met
 + Leu211Asp
 Gly196Ser + Val197Met + Asn198Ser + Thr202Asn + Thr207Asp
 + Asn212Gln
 50 Pro195Gly + Gly196Pro + Thr202Asn + Tyr203Ile + Gly213Asp
 + Thr214Asn
 Pro195Gly + Gly196Pro + Gln200Glu + Pro204Ser + Tyr208Ile
 + Gly213Ser
 Val199Ala + Thr202Gln + Gly205Ser + Ala209Asn + Ser210Glu

+ Leu211Cys
 Ala194His + Pro195Ser + Val199Thr + Gln200Glu + Tyr203Pro
 + Tyr208Cys
 Gly196Gln + Pro204Gly + Ser206Asp + Thr207Pro + Ala209Gln
 5 + Gly213Ser
 Pro195Asn + Thr202Asn + Pro204Asn + Ala209Gln + Asn212Asp
 + Gly213Gln
 Gly196Ser + Asn198Gln + Tyr203His + Asn212Ser + Gly213Asp
 + Thr214Gly
 10 Ala194Gln + Val197Pro + Val199Gln + Gln200Asn + Tyr208Glu
 + Thr214Ser
 Val199Cys + Gln200Asn + Pro204Gly + Ser206Asp + Thr207Ser
 + Asn212Ser
 Ala194Gln + Gly196Gln + Val199His + Thr202Pro + Tyr203Thr
 15 + Gly205Ser
 Asn198Gln + Val199Gly + Thr202Ser + Ser210Asp + Asn212Ser
 + Gly213Gln
 Val199Thr + Gln200Asn + Pro204Ser + Tyr208Val + Asn212Gln
 + Thr214Asp
 20 Ala194His + Gly196Gln + Val199Gln + Thr202Gly + Pro204Asp
 + Leu211Cys
 Ala194Ser + Val197Gly + Pro204Gln + Ala209Pro + Ser210Glu
 + Thr214Gly
 Ala194Gln + Gly196Pro + Tyr203Gln + Thr207Pro + Tyr208Pro
 25 + Ala209Asn
 Gly196Ser + Thr202Asn + Tyr208Ile + Ala209Gln + Leu211Ala
 + Gly213Glu
 Pro195Asn + Gly196Pro + Val197Glu + Gln200Asn + Tyr203Ser
 + Tyr208Ser
 30 Gly196Ser + Val199His + Gly205Asp + Tyr208Val + Ala209Gly
 + Thr214Pro
 Val197Ser + Val199Met + Gln200Asn + Thr202Ser + Tyr208Cys
 + Gly213Gln
 Ala194Ser + Gly196Gln + Val199Pro + Leu211Val + Gly213Glu
 35 + Thr214Gly
 Ala194Gln + Asn198Gln + Val199Cys + Thr207Gly + Leu211Asp
 + Asn212Glu
 Ala194Thr + Asn198Gln + Thr202Asn + Pro204Ser + Gly213Glu
 + Thr214Asp
 40 Ala194Thr + Pro195Ser + Val199Ala + Ala209Glu + Ser210Glu
 + Leu211Cys
 Tyr203Leu + Gly205Ser + Ala209Glu + Ser210Glu + Asn212Ser
 + Gly213Asn
 Val197Glu + Asn198Glu + Tyr203Pro + Thr207Gly + Ala209Ser
 45 + Asn212Ser
 Val197Asp + Asn198Asp + Val199His + Thr202Ser + Pro204Gln
 + Ala209Asn
 Gly196Asn + Val197Glu + Asn198Asp + Gln200Ser + Pro204Asn
 + Thr207Gly
 50 Pro195Gln + Thr202Ser + Tyr203Ser + Thr207Gln + Asn212Asp
 + Gly213Glu
 Gly196Gln + Tyr203His + Gly205Ser + Leu211Asn + Asn212Asp
 + Gly213Glu
 Asn198Ser + Gly205Ser + Tyr208Ile + Asn212Glu + Gly213Glu

+ Thr214Pro
 Ala194Ser + Gly196Gln + Pro204Glu + Gly205Asp + Tyr208Asn
 + Thr214Asn
 Ala194Ser + Pro195Gly + Val199Cys + Pro204Asp + Gly205Glu
 5 + Asn212Gln
 Ala194Thr + Val199Pro + Gly205Asn + Ala209Gln + Ser210Glu
 + Leu211Asp
 Thr202Gln + Thr207Gly + Ser210Asp + Leu211Glu + Gly213Gln
 + Thr214Ser
 10 Thr202Gln + Gly205Asp + Ser206Glu + Tyr206Met + Gly213Gln
 + Thr214Asn
 Ala194Gly + Gly205Glu + Ser206Glu + Ala209Gly + Leu211Gln
 + Thr214Gly
 Gln200Ser + Thr202Ser + Tyr203Gly + Gly205Asp + Ser206Glu
 15 + Thr214Gln
 Val197Asn + Thr202Ser + Gly205Glu + Ser206Glu + Ala209His
 + Thr214Ser
 Ala194Gln + Thr202Ser + Tyr203Gly + Ser206Asp + Thr207Glu
 + Gly213Ser
 20 Gly196Pro + Val199Gln + Tyr203Met + Ser206Glu + Thr207Asp
 + Ala209Thr
 Pro195Gly + Gly196Pro + Thr202Ser + Pro204Gln + Tyr208Asp
 + Ala209Glu
 Pro195Gln + Gly196Pro + Val197Pro + Gln200Asp + Gly205Ser
 25 + Ser210Asp
 Gly196Ser + Asn198Glu + Gly205Pro + Ala209His + Ser210Glu
 + Asn212Gln
 Ala194Thr + Asn198Asp + Thr202Ser + Tyr203Cys + Ala209Pro
 + Ser210Glu
 30 Gly196Pro + Asn198Glu + Gly205Ser + Ser210Glu + Leu211Asn
 + Thr214Asn
 Ala194Pro + Gly196Ser + Asn198Glu + Gly205Ser + Thr207Pro
 + Ser210Glu
 Gly196Ser + Val197His + Asn198Asp + Gln200Ser + Thr207Gln
 35 + Ser210Asp
 Asn198Glu + Val199Met + Gly205Pro + Ala209His + Ser210Glu
 + Thr214Pro
 Val197Ser + Asn198Glu + Pro204Ser + Thr207Ser + Ala209Pro
 + Leu211Asp
 40 Pro195Ser + Gln200Asp + Thr202Asn + Tyr203Ser + Ala209Asp
 + Asn212Ser
 Gln200Asp + Pro204Ser + Gly205Pro + Tyr208His + Ala209Asp
 + Leu211Asn
 Pro204Glu + Ser206Asp + Tyr208Ile + Leu211Gly + Asn212Gln
 45 + Thr214Asn
 Gly196Ser + Asn198Ser + Val199Ala + Pro204Asp + Ser206Glu
 + Tyr208Ser
 Pro195Asn + Pro204Asp + Ser206Asp + Tyr208Ser + Leu211Ser
 + Asn212Gln
 50 Ala194Gly + Asn198Glu + Gln200Ser + Thr207Gly + Ala209Asn
 + Asn212Glu
 Asn198Glu + Gly205Gln + Ala209Pro + Leu211Cys + Asn212Asp
 + Gly213Pro
 Ala194Thr + Val197Thr + Asn198Gln + Pro204Gly + Gly205Asp

+ Thr207Asp
 Ala194Asn + Gly196Pro + Pro204Asp + Thr207Asp + Tyr208Cys
 + Gly213Asn
 Ala194Thr + Pro195Gln + Gln200Ser + Pro204Glu + Thr207Asp
 5 + Gly213Pro
 Val197Pro + Asn198Glu + Gln200Asp + Leu211Ala + Asn212Ser
 + Gly213Pro
 Asn198Asp + Gln200Glu + Tyr203Val + Leu211Thr + Asn212Ser
 + Gly213Pro
 10 Pro195Gln + Asn198Asp + Val199Gln + Gln200Glu + Pro204Asn
 + Ala209Pro
 Ala194Gly + Gly196Asn + Asn198Asp + Gln200Asp + Thr207Gly
 + Asn212Ser
 Gln200Asp + Thr202Asn + Tyr203Ala + Thr207Gln + Leu211Glu
 15 + Thr214Pro
 Val197Asp + Val199His + Tyr203Val + Tyr208His + Leu211Asp
 + Gly213Pro
 Pro195Asn + Val197Gln + Val199Gln + Thr207Asp + Ala209Glu
 + Gly213Ser
 20 Asn198Gln + Gln200Asn + Tyr203Ala + Thr207Asp + Tyr208Val
 + Ala209Asp
 Val197Ala + Asn198Gln + Pro204Ser + Tyr208Thr + Ser210Glu
 + Asn212Glu
 Gly196Asn + Gln200Asn + Pro204Gln + Ser210Asp + Asn212Glu
 25 + Thr214Pro
 Pro195Gln + Val199Pro + Ser210Asp + Asn212Glu + Gly213Asn
 + Thr214Gly
 Pro195Gly + Gln200Ser + Thr207Pro + Tyr208Gln + Ser210Glu
 + Asn212Glu
 30 Pro195Gly + Val199Cys + Thr202Asn + Tyr208His + Ser210Glu
 + Asn212Asp
 Val199His + Thr202Gly + Pro204Gln + Ala209Thr + Ser210Asp
 + Asn212Asp
 Asn198Gln + Thr202Pro + Ala209Ser + Ser210Glu + Asn212Glu
 35 + Gly213Pro
 Ala194Ser + Val199Gln + Tyr208Gly + Ser210Asp + Leu211Gln
 + Asn212Asp
 Ala194Asn + Val199Gly + Gly205Ser + Ala209His + Ser210Glu
 + Asn212Glu
 40 Ala194Ser + Thr202Asn + Pro204Gly + Tyr208Glu + Ser210Glu
 + Gly213Gln
 Pro195Gln + Val199Asn + Thr207Gly + Tyr208Asp + Ser210Asp
 + Leu211Ile
 Pro195Gln + Gln200Asn + Tyr203Gln + Tyr208Glu + Ser210Glu
 45 + Asn212Gln
 Ala194His + Tyr203Asn + Tyr208Asp + Ser210Asp + Leu211His
 + Thr214Ser
 Gly196Asn + Val197Gln + Thr202Asn + Tyr208Glu + Ala209Asn
 + Ser210Glu
 50 Ala194Asn + Gln200Ser + Tyr203Met + Ser206Glu + Tyr208Glu
 + Leu211Val
 Asn198Ser + Pro204Gly + Ser206Glu + Tyr208Asp + Asn212Gln
 + Thr214Gly
 Ala194Pro + Gln200Asn + Thr202Pro + Tyr203Met + Asn212Asp

+ Thr214Asp
 Pro195Ser + Asn198Glu + Gln200Ser + Thr202Asn + Gly205Pro
 + Gly213Asp
 Pro195Ser + Asn198Glu + Val199Ala + Ala209Glu + Leu211Asn
 5 + Thr214Gly
 Pro195Gly + Asn198Glu + Gln200Asn + Thr202Pro + Tyr203Ile
 + Ala209Glu
 Val197Ser + Asn198Asp + Tyr203Pro + Tyr208Met + Ala209Asp
 + Leu211Gln
 10 Pro195Ser + Asn198Asp + Gln200Ser + Tyr208Met + Ala209Asp
 + Leu211Met
 Gly196Asn + Val197Asp + Val199Gln + Gln200Glu + Gly205Asn
 + Gly213Pro
 Gln200Glu + Thr202Gln + Tyr203Met + Ala209Asn + Leu211Ala
 15 + Asn212Asp
 Ala194Pro + Gly196Pro + Gln200Asp + Thr202Asn + Tyr208Ser
 + Asn212Glu
 Val197Gly + Val199Ser + Gln200Glu + Tyr203Gly + Asn212Glu
 + Gly213Pro
 20 Pro204Asp + Thr207Gln + Tyr208Leu + Ala209Asp + Asn212Ser
 + Thr214Asn
 Ala194Ser + Pro195Gln + Thr202Ser + Pro204Asp + Ala209Asp
 + Thr214Asn
 Pro195Asn + Thr202Ser + Tyr203Leu + Tyr208Asp + Ala209His
 25 + Leu211Asp
 Ala194Asn + Gly196Pro + Ser206Glu + Tyr208His + Ala209Asp
 + Thr214Gly
 Pro204Gln + Gly205Asn + Ser206Glu + Thr207Gly + Ala209Asp
 + Leu211Cys
 30 Val197Gln + Thr202Gln + Pro204Gly + Ser206Asp + Ala209Asp
 + Thr214Ser
 Ala194Gly + Val197Gln + Asn198Gln + Tyr203Val + Ser206Asp
 + Ala209Asp
 Gly196Ser + Val197Asn + Gln200Asp + Thr202Pro + Thr207Asp
 35 + Asn212Gln
 Ala194Gly + Gly196Ser + Ser210Asp + Leu211Ser + Asn212Gln
 + Gly213Glu
 Val197Thr + Tyr203His + Thr207Gln + Tyr208Pro + Ser210Asp
 + Gly213Asp
 40 Asn198Ser + Val199Cys + Tyr203Val + Gly205Ser + Ser210Asp
 + Gly213Asp
 Val197His + Val199Asn + Pro204Gln + Ser210Asp + Asn212Ser
 + Gly213Asp
 Gly196Ser + Val197Ala + Gln200Asn + Thr202Pro + Ser210Glu
 45 + Gly213Glu
 Asn198Glu + Tyr203Gly + Gly205Gln + Thr207Pro + Tyr208Val
 + Thr214Glu
 Ala194Gly + Gly196Asn + Asn198Asp + Tyr203Leu + Tyr208His
 + Thr214Glu
 50 Pro195Gly + Asn198Glu + Val199Cys + Ala209Gln + Asn212Gln
 + Thr214Asp
 Asn198Asp + Val199Asn + Thr202Asn + Pro204Gln + Asn212Gln
 + Thr214Asp
 Val199Pro + Gln200Asp + Tyr203Asn + Leu211Pro + Gly213Glu

+ Thr214Asn
 Pro195Ser + Gly196Pro + Val199Ala + Gln200Asp + Asn212Gln
 + Gly213Asp
 Ala194Thr + Pro195Gly + Gly196Pro + Gln200Glu + Gly205Asn
 5 + Gly213Glu
 Val199His + Gln200Glu + Pro204Ser + Leu211His + Gly213Glu
 + Thr214Gln
 Asn198Asp + Gln200Ser + Gly205Ser + Tyr208Asp + Leu211Ala
 + Asn212Ser
 10 Ala194Ser + Asn198Asp + Thr202Ser + Tyr208Asp + Ala209Pro
 + Gly213Gln
 Gln200Asn + Tyr203Pro + Pro204Glu + Gly205Pro + Ser210Asp
 + Leu211Pro
 Val197Ser + Tyr203Pro + Pro204Asp + Ala209Gly + Ser210Asp
 15 + Thr214Asn
 Gly196Asn + Pro204Glu + Ser210Glu + Leu211Pro + Asn212Ser
 + Thr214Gly

TABLE 29

	Loop 6 - Heptuple Mutation Variants
20	Pro195Ser + Asn198Ser + Val199Met + Ser206Glu + Thr207Ser + Gly213Asn + Thr214Gln
	Ala194Gln + Pro195Asn + Val197Ser + Thr202Ser + Tyr203Ser + Ala209Ser + Asn212Asp
25	Val197Asp + Gln200Asn + Thr202Pro + Gly205Gln + Thr207Gly + Tyr208Met + Leu211Val
	Ala194Ser + Pro195Gly + Asn198Ser + Thr202Pro + Ser206Glu + Tyr208Ala + Thr214Gln
	Ala194Pro + Pro195Asn + Thr202Gly + Tyr203Thr + Ser206Glu 30 + Leu211Ser + Thr214Pro
	Gly196Gln + Val197Thr + Gln200Asn + Tyr203Cys + Gly205Ser + Ser210Glu + Leu211Val
	Ala194His + Val199Ser + Thr202Gly + Thr207Asn + Leu211Met + Gly213Glu + Thr214Pro
35	Val199Gly + Tyr203Cys + Pro204Gly + Thr207Asn + Ala209His + Asn212Asp + Gly213Asn
	Ala194Gln + Gly196Pro + Tyr203Ser + Pro204Ser + Tyr208Ser + Leu211Glu + Thr214Pro
	Gly196Gln + Gly205Asn + Thr207Asp + Tyr208Met + Asn212Gln 40 + Gly213Ser + Thr214Pro
	Gly196Gln + Val199Cys + Ser206Glu + Thr207Pro + Ala209Pro + Leu211Ile + Gly213Ser
	Thr202Pro + Tyr203Val + Pro204Asn + Ser206Asp + Asn212Ser + Gly213Ser + Thr214Gly
45	Ala194Thr + Pro195Asn + Gly196Pro + Gln200Asn + Pro204Ser + Asn212Glu + Gly213Gln
	Asn198Gln + Gln200Ser + Pro204Gln + Gly205Asn + Thr207Glu + Asn212Ser + Gly213Ser
	Ala194Ser + Gly196Ser + Asn198Ser + Tyr203Gly + Gly205Pro 50 + Ser206Glu + Gly213Pro
	Ala194Thr + Gly196Gln + Val197Pro + Thr202Gln + Pro204Ser + Ala209Gly + Asn212Glu

Pro195Gln + Gly196Pro + Asn198Gln + Pro204Ser + Gly205Glu
 + Tyr208Gln + Gly213Asn
 Val199Thr + Tyr203Gln + Pro204Gln + Gly205Asn + Thr207Glu
 + Leu211Thr + Thr214Gln
 5 Val197Thr + Asn198Glu + Thr202Gly + Gly205Pro + Thr207Pro
 + Tyr208Met + Gly213Gln
 Pro195Gly + Gly196Ser + Thr202Gly + Tyr203Gln + Pro204Gln
 + Tyr208Pro + Thr214Gln
 Pro195Asn + Asn198Asp + Gln200Ser + Pro204Gly + Gly205Gln
 10 + Tyr208Gly + Ala209Asn
 Pro195Asn + Val199His + Pro204Asn + Ala209Pro + Leu211Thr
 + Asn212Ser + Thr214Pro
 Asn198Gln + Val199Thr + Gln200Asp + Pro204Asn + Leu211Val
 + Asn212Ser + Gly213Gln
 15 Pro195Ser + Gly196Ser + Val197Met + Val199Gly + Gly205Pro
 + Ser210Glu + Asn212Gln
 Ala194Thr + Pro195Gln + Asn198Gln + Thr202Asn + Thr207Asp
 + Tyr208Thr + Gly213Ser
 Pro195Gln + Gly196Asn + Gly205Glu + Thr207Pro + Tyr208Asn
 20 + Ala209His + Asn212Ser
 Asn198Gln + Thr202Pro + Thr207Pro + Leu211Pro + Asn212Glu
 + Gly213Asn + Thr214Ser
 Ala194Pro + Val197Met + Pro204Ser + Thr207Gln + Tyr208Asn
 + Ala209Gln + Thr214Gly
 25 Ala194Asn + Val197Cys + Pro204Asn + Tyr208Thr + Ala209Pro
 + Ser210Glu + Leu211Ser
 Gly196Asn + Val197Gly + Tyr203Pro + Gly205Asp + Leu211Ala
 + Gly213Asn + Thr214Ser
 Ala194Thr + Pro195Asn + Tyr203Pro + Gly205Ser + Ser210Glu
 30 + Leu211Ala + Gly213Pro
 Ala194His + Gly196Asn + Val197Met + Asn198Ser + Ser206Asp
 + Leu211Asn + Asn212Ser
 Ala194Thr + Gly196Ser + Val199Ser + Thr202Asn + Ala209Pro
 + Leu211Pro + Gly213Gln
 35 Gly196Gln + Val199His + Thr202Pro + Tyr203Thr + Pro204Asp
 + Gly205Ser + Ala209Asn
 Val197Cys + Val199Gly + Thr202Gln + Tyr203His + Gly205Glu
 + Tyr208Ile + Thr214Gln
 Ala194Gly + Val197Cys + Asn198Asp + Gln200Ser + Tyr203Leu
 40 + Ala209Gln + Asn212Gln
 Ala194Gly + Tyr203Cys + Gly205Gln + Ser206Glu + Tyr208Met
 + Leu211Cys + Thr214Gly
 Gly196Ser + Val199Gln + Thr202Ser + Tyr203His + Pro204Gln
 + Tyr208Leu + Gly213Pro
 45 Asn198Gln + Thr202Asn + Tyr203Ala + Pro204Glu + Tyr208Gly
 + Ala209Gln + Thr214Gln
 Ala194Asn + Pro195Gln + Pro204Gly + Ser206Glu + Thr207Ser
 + Tyr208Ala + Asn212Ser
 Ala194Pro + Pro195Gln + Val197Ser + Asn198Ser + Gln200Glu
 50 + Thr202Ser + Gly205Ser
 Pro195Ser + Gly196Ser + Val199Gly + Thr202Gly + Pro204Glu
 + Leu211Ala + Thr214Asn
 Ala194Thr + Gly196Pro + Asn198Ser + Pro204Asn + Tyr208Gly
 + Ser210Asp + Thr214Asn

Ala194Pro + Val199Asn + Thr202Gln + Pro204Gln + Gly205Asp
 + Thr207Ser + Ala209Pro
 Ala194Pro + Pro195Gly + Val197Cys + Val199Gln + Tyr203Cys
 + Tyr208His + Gly213Glu
 5 Val197Asp + Val199Ser + Gly205Pro + Thr207Gly + Leu211Thr
 + Asn212Gln + Gly213Ser
 Ala194Pro + Pro195Ser + Gln200Asn + Thr202Pro + Tyr208His
 + Gly213Asp + Thr214Gly
 Ala194Thr + Val197Asn + Val199Pro + Gln200Asp + Thr202Ser
 10 + Thr207Asn + Tyr208Leu
 Pro195Ser + Gly196Gln + Val197Ala + Thr202Gln + Tyr203Gly
 + Tyr208Cys + Gly213Asn
 Ala194Gln + Val199Gln + Thr202Gly + Pro204Asn + Gly205Glu
 + Ala209His + Leu211His
 15 Pro195Asn + Val199Thr + Tyr203Gly + Gly205Gln + Ser206Asp
 + Asn212Ser + Gly213Pro
 Ala194Gln + Pro195Ser + Gly196Gln + Thr202Gln + Ala209His
 + Asn212Ser + Thr214Glu
 Gly196Pro + Val197Cys + Tyr203Pro + Gly205Ser + Ser206Asp
 20 + Leu211Ile + Thr214Gly
 Gly196Asn + Val197Gly + Val199His + Thr202Ser + Ala209His
 + Asn212Glu + Thr214Gln
 Gly196Gln + Gln200Ser + Thr202Gln + Gly205Gln + Ala209Ser
 + Gly213Asp + Thr214Glu
 25 Val199Gly + Gln200Asn + Thr202Gln + Gly205Ser + Ala209Glu
 + Ser210Asp + Leu211Asn
 Val199Pro + Gln200Asn + Tyr203Val + Ala209Asp + Ser210Asp
 + Leu211Ser + Gly213Pro
 Ala194Gly + Tyr203Val + Gly205Asn + Thr207Gly + Ala209Glu
 30 + Ser210Asp + Leu211Pro
 Pro195Gln + Thr202Gly + Tyr203Val + Ala209Glu + Ser210Glu
 + Gly213Ser + Thr214Gln
 Pro195Asn + Val197Ser + Tyr208Thr + Ala209Glu + Ser210Asp
 + Asn212Ser + Thr214Gln
 35 Ala194Asn + Gly196Ser + Val199Gly + Thr202Pro + Tyr203Leu
 + Asn212Glu + Gly213Asp
 Val197Cys + Asn198Ser + Gln200Ser + Thr202Asn + Thr207Gln
 + Asn212Asp + Gly213Asp
 Gly196Pro + Thr202Asn + Pro204Asp + Gly205Glu + Ala209His
 40 + Leu211His + Gly213Ser
 Pro195Gly + Gly196Gln + Tyr203Thr + Thr207Asn + Ser210Asp
 + Leu211Asp + Asn212Ser
 Ala194Gly + Gly196Pro + Thr202Gln + Tyr203Val + Gly205Ser
 + Ser210Asp + Leu211Asp
 45 Ala194His + Val199Cys + Tyr203Ala + Tyr208Gly + Ser210Asp
 + Leu211Asp + Gly213Pro
 Ala194His + Gly196Ser + Val197Cys + Val199Ser + Gly205Glu
 + Ser206Glu + Tyr208Ser
 Ala194His + Gly196Ser + Val197Thr + Val199Cys + Gly205Asp
 50 + Ser206Glu + Thr214Gln
 Thr202Asn + Tyr203Thr + Gly205Glu + Ser206Asp + Ala209Gln
 + Leu211Thr + Thr214Gly
 Ala194Pro + Val197Met + Asn198Ser + Val199Asn + Thr202Ser
 + Ser206Asp + Thr207Glu

Pro195Asn + Val199Met + Thr202Gly + Ser206Glu + Thr207Asp
 + Tyr208Thr + Asn212Ser
 Pro195Gly + Gly196Asn + Val199Gln + Tyr203His + Ser206Glu
 + Thr207Asp + Asn212Gln
 5 Pro195Asn + Val199Ala + Gly205Pro + Ser206Glu + Thr207Asp
 + Tyr208Gly + Asn212Ser
 Pro195Asn + Gly196Ser + Val197Ala + Pro204Ser + Ser206Glu
 + Thr207Asp + Asn212Gln
 Pro195Asn + Val197Thr + Ser206Asp + Thr207Asp + Leu211Thr
 10 + Gly213Ser + Thr214Ser
 Ala194Thr + Val197Cys + Asn198Ser + Thr207Asp + Tyr208Asp
 + Asn212Ser + Gly213Asn
 Ala194Thr + Gln200Asp + Thr202Gln + Ala209His + Ser210Asp
 + Leu211Gly + Thr214Gly
 15 Pro195Gln + Gln200Asp + Tyr203Ala + Gly205Asn + Tyr208Ser
 + Ser210Asp + Gly213Asn
 Ala194Thr + Val199Pro + Gln200Glu + Thr207Gly + Ser210Glu
 + Leu211Ser + Gly213Asn
 Val197Ser + Gln200Glu + Tyr203Leu + Pro204Asn + Ala209Gly
 20 + Ser210Asp + Leu211Asn
 Gly196Gln + Asn198Gln + Val199Pro + Gln200Asp + Thr202Gly
 + Pro204Gly + Ser210Asp
 Asn198Gln + Val199Cys + Gln200Glu + Gly205Gln + Ser210Asp
 + Gly213Ser + Thr214Gly
 25 Asn198Gln + Gln200Glu + Gly205Pro + Thr207Ser + Ala209Asn
 + Ser210Glu + Thr214Asn
 Gln200Glu + Thr202Asn + Thr207Ser + Tyr208Pro + Ser210Glu
 + Gly213Gln + Thr214Gly
 Ala194Pro + Pro195Ser + Gly196Asn + Val197Asp + Val199Thr
 30 + Pro204Gly + Asn212Glu
 Gly196Asn + Asn198Glu + Tyr203Gly + Pro204Gln + Ser210Asp
 + Leu211Val + Asn212Ser
 Gly196Pro + Val197Gly + Asn198Asp + Thr202Pro + Tyr203Val
 + Thr207Asn + Ser210Glu
 35 Pro195Asn + Gly196Pro + Asn196Asp + Thr202Ser + Pro204Gln
 + Ser210Asp + Gly213Gln
 Pro195Ser + Val197Pro + Asn198Glu + Val199Met + Thr207Ser
 + Ser210Asp + Thr214Gln
 Ala194Ser + Gly196Asn + Val197Met + Asn198Asp + Val199Thr
 40 + Tyr208Met + Leu211Glu
 Asn198Asp + Val199Gln + Pro204Ser + Leu211Asp + Asn212Ser
 + Gly213Pro + Thr214Asn
 Pro195Gln + Asn196Asp + Thr202Pro + Gly205Gln + Tyr208Met
 + Leu211Glu + Gly213Asn
 45 Gly196Pro + Gln200Asp + Thr202Ser + Tyr203Thr + Tyr208His
 + Ala209Glu + Leu211Ile
 Ala194Thr + Gln200Asn + Thr202Pro + Pro204Asp + Ser206Glu
 + Thr207Asn + Ala209Ser
 Gly196Pro + Pro204Asp + Gly205Ser + Ser206Asp + Tyr208Gly
 50 + Gly213Gln + Thr214Gly
 Pro195Gln + Val197Gln + Gln200Ser + Pro204Glu + Ser206Asp
 + Ala209Gly + Thr214Gln
 Ala194Thr + Pro195Gly + Val197Pro + Pro204Asp + Ser206Glu
 + Leu211Val + Gly213Ser

Pro195Asn + Gly196Ser + Pro204Glu + Ser206Asp + Thr207Gly
 + Tyr208Val + Ala209Thr
 Pro195Asn + Gly196Pro + Val197Gln + Asn198Asp + Tyr203Gln
 + Tyr208Asn + Asn212Asp
 5 Gly196Gln + Val197Thr + Asn198Asp + Val199Gly + Thr202Pro
 + Tyr208Asn + Asn212Glu
 Pro195Asn + Asn198Asp + Val199Asn + Thr202Gln + Ala209Pro
 + Asn212Asp + Gly213Gln
 Ala194Gly + Val197Met + Asn198Asp + Gln200Glu + Thr202Asn
 10 + Pro204Asn + Tyr208Asn
 Pro195Ser + Val197Gln + Asn198Glu + Val199Cys + Gln200Asp
 + Gly205Ser + Ala209Pro
 Pro195Gln + Gly196Pro + Asn198Glu + Val199Ser + Gln200Asp
 + Gly205Ser + Thr214Asn
 15 Ala194Gln + Pro195Ser + Asn198Glu + Gln200Asp + Thr207Gln
 + Tyr208Leu + Asn212Gln
 Ala194Pro + Pro195Asn + Gln200Glu + Pro204Gln + Thr207Gln
 + Tyr208Asp + Gly213Gln
 Val199Thr + Gln200Asp + Tyr208Glu + Ala209Thr + Leu211Ser
 20 + Asn212Ser + Gly213Asn
 Gly196Pro + Val197Glu + Asn198Gln + Val199Met + Tyr208Met
 + Gly213Asp + Thr214Asn
 Pro195Gly + Val197Glu + Val199Thr + Gln200Ser + Gly205Asn
 + Ala209Gly + Leu211Glu
 25 Val197Met + Val199Cys + Gly205Pro + Tyr208Ile + Leu211Asp
 + Asn212Ser + Gly213Asp
 Pro195Gln + Asn198Ser + Val199Gln + Pro204Ser + Ser210Asp
 + Leu211Cys + Asn212Glu
 Pro195Ser + Gly196Pro + Asn198Gln + Pro204Gln + Ala209Thr
 30 + Ser210Glu + Asn212Glu
 Ala194Gly + Asn198Gln + Val199Gln + Thr207Ser + Ser210Asp
 + Leu211Gly + Asn212Asp
 Ala194Gln + Val197Gly + Thr202Ser + Pro204Ser + Ser210Glu
 + Asn212Glu + Gly213Ser
 35 Ala194Asn + Asn198Ser + Thr202Pro + Ser210Glu + Leu211Cys
 + Asn212Asp + Gly213Ser
 Pro195Gly + Val197Thr + Thr202Asn + Gly205Ser + Ser210Asp
 + Asn212Glu + Gly213Ser
 Pro195Gln + Gly205Gln + Ala209Gln + Ser210Asp + Leu211Asn
 40 + Asn212Glu + Thr214Gln
 Val199His + Pro204Asn + Tyr208Ile + Ala209Thr + Ser210Glu
 + Leu211Gln + Asn212Asp
 Val197Asn + Asn198Gln + Tyr203Pro + Pro204Asn + Ser210Glu
 + Asn212Glu + Thr214Gln
 45 Ala194Pro + Gly196Ser + Gln200Ser + Gly205Gln + Tyr208Gly
 + Ser210Glu + Asn212Glu
 Pro195Ser + Val197Gly + Asn198Gln + Val199Gln + Gln200Ser
 + Ser210Glu + Asn212Asp
 Asn198Gln + Gln200Asn + Thr207Gly + Tyr208Glu + Ser210Glu
 50 + Asn212Ser + Thr214Asn
 Pro195Gly + Thr202Ser + Tyr208Glu + Ala209Asn + Ser210Glu
 + Asn212Gln + Thr214Asn
 Val199Thr + Thr202Ser + Gly205Pro + Ser206Glu + Tyr208Glu
 + Leu211His + Asn212Ser

Ala194Gln + Gly196Pro + Asn198Gln + Tyr203Ile + Ser206Asp
 + Tyr208Asp + Gly213Gln
 Ala194Ser + Pro195Ser + Thr202Ser + Gly205Gln + Ser206Asp
 + Tyr208Asp + Asn212Gln
 5 Pro195Gly + Val197His + Tyr203Gln + Thr207Pro + Asn212Asp
 + Gly213Ser + Thr214Asp
 Pro195Gly + Val197Met + Thr202Asn + Tyr208Met + Leu211Thr
 + Asn212Glu + Thr214Asp
 Val197Ser + Asn198Gln + Thr202Ser + Pro204Glu + Thr207Ser
 10 + Tyr208Asp + Ala209Ser
 Ala194Pro + Val199Asn + Pro204Asp + Tyr208Glu + Leu211Gly
 + Asn212Gln + Gly213Ser
 Pro195Gln + Val197Glu + Val199Gly + Gln200Ser + Thr207Ser
 + Ser210Glu + Leu211Asn
 15 Pro195Ser + Val197Asp + Val199Cys + Pro204Gly + Tyr208Ser
 + Ser210Glu + Asn212Ser
 Ala194Gln + Val197Asp + Asn198Ser + Thr202Asn + Thr207Asn
 + Ser210Glu + Leu211His
 Val197Asp + Gln200Asn + Tyr203Thr + Tyr208Val + Ser210Asp
 20 + Asn212Ser + Thr214Ser
 Ala194Pro + Val197Asp + Gln200Ser + Thr202Gly + Leu211Cys
 + Gly213Asn + Thr214Glu
 Pro195Ser + Val197Glu + Asn198Gln + Tyr208Ile + Ala209His
 + Leu211Val + Thr214Glu
 25 Pro195Gly + Val197Asp + Gln200Ser + Thr202Pro + Ala209Thr
 + Gly213Gln + Thr214Asp
 Pro195Asn + Gly196Pro + Asn198Asp + Pro204Asn + Gly205Asn
 + Ala209Asn + Gly213Asp
 Ala194Pro + Asn198Asp + Val199Gln + Gln200Ser + Thr207Pro
 30 + Ala209Asp + Gly213Asn
 Val197Asp + Val199His + Gln200Glu + Thr202Pro + Tyr203Ile
 + Thr207Gly + Thr214Gly
 Val197Glu + Gln200Asp + Tyr203Ile + Pro204Gln + Ala209Gly
 + Leu211Ile + Thr214Pro
 35 Pro195Asn + Gly196Ser + Val199Met + Gln200Asp + Tyr203Ala
 + Asn212Asp + Gly213Asn
 Ala194Thr + Gly196Gln + Gln200Glu + Tyr203Val + Tyr208Ala
 + Leu211Ala + Asn212Glu
 Val197Asn + Asn198Gln + Pro204Asp + Tyr208Met + Ala209Glu
 40 + Asn212Ser + Gly213Asn
 Pro195Asn + Thr202Gly + Tyr203Asn + Pro204Glu + Gly205Asn
 + Thr207Ser + Ala209Glu
 Ala194Pro + Gly196Pro + Tyr203Ala + Thr207Gln + Leu211Glu
 + Gly213Pro + Thr214Glu
 45 Asn198Gln + Val199Thr + Thr202Pro + Pro204Gln + Ala209Thr
 + Leu211Glu + Thr214Asp
 Ala194His + Val199Cys + Gln200Glu + Tyr203Ile + Gly205Asn
 + Thr207Glu + Tyr208Met
 Val199Pro + Gln200Asp + Pro204Gln + Gly205Asn + Thr207Asp
 50 + Tyr208Cys + Thr214Pro
 Ala194His + Pro195Gln + Gly196Gln + Val199His + Gln200Glu
 + Thr207Glu + Asn212Ser
 Ala194Gly + Asn198Gln + Gln200Asn + Tyr203Leu + Ser210Asp
 + Leu211Gly + Gly213Glu

Asn198Gln + Gln200Asn + Thr202Ser + Ser210Asp + Leu211Ser
 + Gly213Glu + Thr214Asn
 Pro195Asn + Val197Met + Tyr203Gly + Gly205Pro + Tyr208His
 + Ser210Asp + Gly213Asp
 5 Pro195Ser + Gln200Asn + Thr207Pro + Ser210Glu + Leu211Met
 + Gly213Glu + Thr214Gln
 Val197Gln + Val199Ser + Thr202Asn + Tyr208Gly + Ala209Gly
 + Ser210Glu + Gly213Asp
 Gln200Asn + Pro204Gln + Thr207Glu + Ala209Ser + Ser210Asp
 10 + Leu211Thr + Gly213Asn
 Ala194Gln + Thr202Gly + Tyr203Asn + Thr207Asp + Ser210Asp
 + Leu211Cys + Gly213Pro
 Pro195Gln + Val199Gln + Gly205Gln + Thr207Glu + Tyr208Ile
 + Ser210Asp + Thr214Gly
 15 Pro195Gly + Val197His + Val199Met + Tyr203Thr + Thr207Glu
 + Ser210Asp + Asn212Gln
 Ala194Gln + Pro195Gln + Asn198Ser + Val199Gln + Pro204Gln
 + Thr207Glu + Ser210Glu
 Val197Pro + Asn198Glu + Val199Thr + Pro204Asn + Leu211Cys
 20 + Asn212Ser + Thr214Asp
 Ala194Ser + Val199Thr + Gln200Glu + Tyr203Cys + Tyr208Gly
 + Leu211Gly + Gly213Glu
 Val199Pro + Gln200Asp + Tyr203Asn + Pro204Gly + Leu211Pro
 + Gly213Glu + Thr214Asn
 25 Ala194Gln + Asn198Glu + Thr207Ser + Tyr208Glu + Asn212Gln
 + Gly213Gln + Thr214Gln
 Pro195Gln + Asn198Asp + Gln200Ser + Gly205Ser + Tyr208Asp
 + Leu211Ala + Asn212Ser
 Gly196Pro + Val197Asp + Asn198Gln + Val199Ala + Pro204Gln
 30 + Ala209Asp + Gly213Asn
 Pro195Ser + Asn198Gln + Val199Gly + Pro204Glu + Ala209Gly
 + Ser210Asp + Asn212Gln
 Pro195Ser + Gln200Ser + Pro204Glu + Thr207Pro + Ala209Gln
 + Ser210Asp + Asn212Gln
 35 Ala194His + Gly196Ser + Val197Gly + Val199Asn + Gln200Glu
 + Pro204Glu + Ala209Thr
 Gly196Pro + Asn198Ser + Pro204Asn + Tyr208Gly + Ala209Asp
 + Leu211Thr + Gly213Asp
 Gly196Pro + Val199Thr + Gln200Asp + Thr202Asn + Tyr203Asn
 40 + Ser206Glu + Ala209Ser
 Pro195Ser + Gly196Pro + Val199Pro + Gln200Glu + Pro204Gln
 + Ser206Asp + Leu211Ala
 Pro195Ser + Gln200Asp + Thr202Gln + Pro204Gln + Ser206Glu
 + Tyr208Gly + Ala209Gly
 45 Gly196Asn + Val199Ser + Gln200Glu + Thr202Pro + Ala209Thr
 + Leu211Cys + Thr214Asp
 Val197Asn + Gln200Glu + Tyr203Gln + Gly205Pro + Ala209Thr
 + Leu211Val + Thr214Glu
 Pro195Gly + Tyr203Gly + Ser206Glu + Tyr208Gly + Ala209Gln
 50 + Ser210Glu + Leu211Ile
 Gly196Asn + Val197His + Val199Ala + Pro204Asn + Ser206Asp
 + Ser210Asp + Leu211Thr
 Ala194Gln + Val197Ser + Val199Pro + Ser206Asp + Ser210Glu
 + Leu211Pro + Thr214Gly

Ala194His + Gln200Ser + Thr202Asn + Ser206Glu + Tyr208Cys
 + Ser210Asp + Asn212Ser
 Val197Thr + Thr202Ser + Pro204Gly + Gly205Asn + Ser206Asp
 + Ser210Glu + Leu211Pro

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TABLE 30

Loop 6 - Octuple Mutation Variants	
	Pro195Ser + Val197Ser + Asn198Ser + Val199Gly + Tyr203Thr + Thr207Asn + Tyr208Met + Asn212Glu
10	Pro195Gln + Gly196Gln + Val199Gln + Tyr203Gln + Tyr208Met + Ala209Gly + Leu211Val + Gly213Asp
	Pro195Gln + Asn198Gln + Val199His + Pro204Gly + Ser206Glu + Thr207Gln + Tyr208Ser + Leu211Gln
15	Ala194Thr + Val197Met + Val199His + Thr202Ser + Tyr203Ile + Thr207Gln + Tyr208Pro + Leu211Gly
	Pro195Gln + Val197Asn + Val199Cys + Tyr203Met + Pro204Asn + Gly205Glu + Thr207Pro + Tyr208Ser
	Gly196Ser + Gln200Asn + Pro204Asp + Gly205Ser + Thr207Pro + Tyr208Met + Gly213Gln + Thr214Ser
20	Val197Gln + Gln200Asn + Tyr203His + Pro204Asp + Gly205Ser + Tyr208Thr + Ala209Gln + Leu211Pro
	Pro195Gly + Gly196Ser + Val197Pro + Val199Ser + Thr202Asn + Ala209Glu + Leu211Ser + Gly213Pro
25	Ala194His + Gly196Ser + Val197Asn + Asn198Ser + Tyr203Leu + Pro204Asn + Thr207Ser + Ala209Thr
	Ala194Pro + Gly196Pro + Val199Met + Gln200Asp + Thr202Asn + Thr207Asn + Ala209Pro + Gly213Pro
	Pro195Asn + Gly196Pro + Val199Thr + Thr202Gln + Thr207Gly + Tyr208Ser + Ser210Asp + Asn212Ser
30	Ala194Thr + Pro195Asn + Gly196Gln + Thr202Pro + Pro204Ser + Gly205Pro + Tyr208Gln + Leu211Asp
	Ala194Gly + Pro195Ser + Val197Ala + Thr202Gly + Tyr203Gly + Pro204Gln + Gly205Ser + Leu211Glu
	Pro195Asn + Val197Glu + Val199Thr + Gln200Asn + Thr202Pro + Tyr203Ile + Pro204Ser + Leu211Cys
35	Ala194His + Pro195Gln + Val199Cys + Gln200Asp + Tyr203Ala + Thr207Ser + Gly213Gln + Thr214Pro
	Ala194Gln + Gly196Gln + Val199His + Thr202Pro + Tyr203Thr + Pro204Asp + Gly205Ser + Ala209Asn
40	Pro195Ser + Gly196Ser + Gln200Asn + Tyr203His + Thr207Pro + Leu211Met + Gly213Glu + Thr214Gln
	Val197Cys + Asn198Ser + Val199Ala + Gln200Asp + Tyr203His + Leu211Asn + Asn212Gln + Gly213Asn
	Ala194Gln + Gly196Pro + Asn198Gln + Val199His + Tyr203Val + Thr207Ser + Ala209Ser + Leu211Asn
45	Pro195Gly + Gly196Ser + Val197Pro + Thr207Gly + Leu211Thr + Asn212Ser + Gly213Asn + Thr214Glu
	Val197Asn + Thr202Gly + Tyr203Ala + Gly205Gln + Tyr208Ile + Ala209Thr + Ser210Asp + Leu211Gly
50	Ala194Asn + Asn198Gln + Val199Ser + Thr202Gly + Tyr203Ile + Ala209Thr + Ser210Asp + Thr214Ser
	Pro195Ser + Gly196Asn + Val197Asn + Asn198Ser + Thr202Asn

+ Tyr203Cys + Tyr208Asn + Leu211Thr
Ala194Gly + Pro195Ser + Gly196Gln + Val199Ala + Thr202Pro
+ Thr207Ser + Asn212Ser + Thr214Asp
Val197Cys + Val199Pro + Thr202Pro + Tyr203Ser + Ser206Glu
5 + Thr207Gln + Ala209Gly + Thr214Gly
Ala194Gly + Pro195Gln + Gly196Gln + Asn198Ser + Val199Met
+ Thr202Pro + Thr207Glu + Thr214Gly
Ala194His + Pro195Gln + Val197Gln + Asn198Gln + Tyr203Ser
+ Ser206Glu + Tyr208Ala + Leu211Ala
10 Ala194Gly + Gly196Ser + Tyr203His + Pro204Asn + Ser206Asp
+ Tyr208Ile + Leu211Gln + Asn212Ser
Gly196Pro + Gln200Ser + Tyr203Gln + Pro204Ser + Gly205Ser
+ Tyr208Cys + Leu211Met + Gly213Gln
Ala194Asn + Tyr203Asn + Gly205Glu + Thr207Gln + Ala209Thr
15 + Leu211His + Gly213Pro + Thr214Gln
Ala194Ser + Pro195Asn + Gly196Asn + Val199Ser + Pro204Ser
+ Gly205Asn + Ala209Asp + Thr214Gln
Pro195Asn + Gly196Gln + Thr202Pro + Gly205Ser + Ser206Glu
+ Tyr208Ser + Ala209Pro + Gly213Gln
20 Ala194Thr + Pro195Gly + Val197Asp + Asn198Gln + Gly205Ser
+ Tyr208Val + Asn212Gln + Gly213Ser
Pro195Gly + Asn198Ser + Tyr203Thr + Pro204Asn + Tyr208Pro
+ Ala209Thr + Asn212Ser + Gly213Ser
Ala194Thr + Pro195Ser + Gly196Asn + Val197Met + Gln200Ser
25 + Thr202Asn + Tyr203His + Tyr208Gln
Ala194His + Asn198Ser + Tyr203Gln + Pro204Gln + Ala209Pro
+ Leu211Asp + Asn212Glu + Gly213Asn
Ala194Asn + Pro195Ser + Val197Gly + Pro204Gly + Gly205Asn
+ Ala209Asp + Ser210Asp + Thr214Gln
30 Gly196Gln + Val197Pro + Gln200Asn + Thr202Asn + Gly205Gln
+ Ala209Glu + Ser210Asp + Thr214Pro
Val197Ser + Val199Ala + Thr202Ser + Tyr203Pro + Gly205Asn
+ Tyr208Ile + Ala209Asp + Ser210Glu
Asn198Ser + Val199Met + Gln200Ser + Pro204Ser + Tyr208Ala
35 + Ala209Glu + Ser210Asp + Leu211Gly
Ala194Gly + Val197Asn + Asn198Ser + Gln200Ser + Tyr203Thr
+ Ala209Asp + Ser210Asp + Thr214Pro
Ala194His + Pro195Ser + Asn198Ser + Tyr203Cys + Thr207Ser
+ Ala209Asp + Ser210Glu + Gly213Ser
40 Pro195Ser + Val199Asn + Gln200Ser + Pro204Ser + Thr207Gly
+ Ala209Asp + Ser210Asp + Asn212Ser
Ala194Gln + Gly196Pro + Val197Asp + Asn198Glu + Val199Ser
+ Gly205Gln + Ala209Gly + Asn212Ser
Pro195Gln + Val197Asp + Asn198Glu + Val199Ala + Gln200Ser
45 + Thr202Ser + Thr207Gly + Tyr208Ala
Pro195Ser + Gly196Pro + Gln200Asn + Thr202Asn + Tyr203Met
+ Thr207Gly + Asn212Asp + Gly213Asp
Gly196Asn + Thr202Pro + Pro204Gly + Thr207Pro + Leu211Cys
+ Asn212Glu + Gly213Glu + Thr214Pro
50 Gly196Asn + Asn198Gln + Gln200Ser + Thr202Pro + Tyr203Cys
+ Pro204Asn + Asn212Asp + Gly213Glu
Asn198Ser + Val199Gly + Tyr203Ala + Pro204Asp + Gly205Glu
+ Tyr208Met + Ala209Ser + Leu211Pro
Val197Cys + Val199Asn + Thr202Gln + Pro204Asp + Gly205Asp

+ Ala209Gln + Leu211Gln + Asn212Ser
 Pro195Asn + Val199Thr + Thr202Gly + Ala209His + Ser210Glu
 + Leu211Asp + Asn212Ser + Gly213Asn
 Gly196Asn + Val199His + Tyr203Ala + Gly205Asp + Ser206Asp
 5 + Thr207Gln + Tyr208Gln + Leu211Asn
 Ala194Gly + Gly196Gln + Val199Gln + Gln200Asn + Pro204Gly
 + Gly205Asp + Ser206Asp + Thr214Ser
 Ala194Gln + Pro195Asn + Val197Ala + Gln200Asn + Tyr203Ser
 + Gly205Asp + Ser206Asp + Tyr208Ala
 10 Ala194Gln + Val197Gln + Pro204Asn + Gly205Asp + Ser206Glu
 + Tyr208Ala + Ala209His + Gly213Asn
 Pro195Ser + Gly196Asn + Val197Thr + Gln200Asn + Pro204Ser
 + Gly205Glu + Ser206Glu + Tyr208Gly
 Val197Gly + Asn198Gln + Val199Met + Gln200Asn + Tyr203His
 15 + Ser206Asp + Thr207Glu + Thr214Pro
 Ala194Gln + Pro195Gly + Gly196Pro + Thr202Pro + Ser206Asp
 + Thr207Asp + Tyr208Val + Ala209His
 Ala194Thr + Pro195Ser + Val197Gln + Asn198Gln + Thr202Ser
 + Pro204Asn + Ser206Glu + Thr207Asp
 20 Ala194Gln + Val199Met + Thr202Ser + Tyr203Gly + Gly205Gln
 + Ser206Asp + Thr207Glu + Gly213Ser
 Ala194Gly + Pro195Asn + Gly196Gln + Tyr203Ala + Ser206Asp
 + Thr207Glu + Ala209Thr + Asn212Gln
 Gly196Ser + Gln200Ser + Tyr203Leu + Pro204Ser + Ser206Glu
 25 + Thr207Glu + Ala209Ser + Gly213Ser
 Ala194Ser + Pro195Asn + Thr202Gln + Ser206Glu + Thr207Glu
 + Tyr208Gly + Asn212Ser + Thr214Gly
 Ala194His + Pro195Gln + Val197Ala + Thr202Asn + Tyr203Pro
 + Gly205Pro + Tyr208Asp + Ala209Asp
 30 Ala194Gln + Pro195Gln + Val197Asn + Gln200Asp + Ala209Gly
 + Ser210Glu + Leu211Ala + Thr214Asn
 Ala194Pro + Val199Met + Gln200Glu + Thr202Gly + Pro204Gln
 + Gly205Asn + Tyr208Gln + Ser210Asp
 Gly196Pro + Val197Cys + Val199Asn + Gln200Glu + Gly205Pro
 35 + Tyr208Val + Ser210Glu + Thr214Pro
 Ala194Thr + Pro195Gly + Gly196Gln + Val197Asp + Val199His
 + Gln200Ser + Thr202Ser + Asn212Asp
 Asn198Asp + Val199Pro + Gly205Asn + Thr207Gly + Tyr208Pro
 + Ser210Asp + Leu211Gly + Gly213Gln
 40 Ala194Gln + Gly196Pro + Asn198Glu + Tyr203Gln + Thr207Gln
 + Tyr208Pro + Ala209Pro + Ser210Glu
 Ala194Pro + Asn198Asp + Val199His + Gly205Asn + Ser210Glu
 + Leu211Asn + Asn212Ser + Thr214Pro
 Asn198Glu + Val199Pro + Tyr203Asn + Thr207Pro + Ala209Asn
 45 + Ser210Glu + Asn212Ser + Gly213Gln
 Ala194Gly + Pro195Asn + Asn198Asp + Tyr203Ala + Gly205Gln
 + Thr207Ser + Ser210Glu + Leu211Val
 Ala194Thr + Asn198Asp + Thr202Gly + Pro204Ser + Gly205Ser
 + Thr207Asn + Ala209Pro + Ser210Glu
 50 Ala194Gln + Asn198Asp + Tyr203Ala + Thr207Gln + Tyr208Pro
 + Ser210Glu + Leu211Pro + Asn212Ser
 Ala194Thr + Pro195Ser + Asn198Asp + Tyr203Cys + Pro204Asn
 + Thr207Gln + Tyr208Gln + Ser210Glu
 Pro195Ser + Asn198Asp + Val199Ser + Gln200Ser + Pro204Ser

+ Ser210Glu + Leu211Gly + Asn212Ser
 Ala194Gln + Pro195Ser + Gly196Pro + Gln200Glu + Pro204Asn
 + Gly205Pro + Ala209Glu + Leu211Cys
 Val199His + Gln200Ser + Pro204Asp + Gly205Ser + Ser206Asp
 5 + Tyr208Gly + Gly213Gln + Thr214Gly
 Gly196Asn + Asn198Ser + Thr202Ser + Pro204Asp + Gly205Ser
 + Ser206Asp + Thr207Ser + Tyr208Val
 Val197Ala + Gln200Asn + Pro204Glu + Gly205Ser + Ser206Glu
 + Tyr208Val + Leu211Ser + Asn212Ser
 10 Pro195Asn + Val197Thr + Thr202Ser + Tyr203Ile + Pro204Asp
 + Ser206Asp + Thr207Gln + Ala209Gln
 Pro195Gly + Val197Asn + Val199Ser + Gln200Asn + Tyr203Asn
 + Pro204Glu + Ser206Glu + Leu211Met
 Gly196Ser + Asn198Ser + Val199Met + Gln200Asn + Pro204Glu
 15 + Ser206Asp + Leu211Val + Thr214Gln
 Ala194Gln + Gly196Asn + Asn198Asp + Gln200Ser + Thr202Asn
 + Pro204Asn + Asn212Glu + Thr214Asn
 Pro195Gly + Asn198Glu + Val199Asn + Gln200Ser + Thr202Gly
 + Thr207Asn + Ala209Thr + Asn212Asp
 20 Pro195Asn + Gly196Ser + Asn198Glu + Thr207Ser + Tyr208Ser
 + Ala209Pro + Asn212Asp + Thr214Asn
 Ala194Pro + Val197Ser + Asn198Glu + Gln200Asn + Tyr203Cys
 + Thr207Pro + Tyr208Thr + Asn212Asp
 Pro195Gly + Gly196Ser + Thr202Asn + Pro204Asn + Gly205Glu
 25 + Thr207Asp + Tyr208Thr + Asn212Ser
 Val197Gln + Val199Asn + Thr202Pro + Gly205Glu + Thr207Glu
 + Tyr208Ala + Leu211Ser + Gly213Asn
 Ala194Ser + Pro195Ser + Val197Gly + Pro204Asp + Gly205Ser
 + Thr207Glu + Tyr208Val + Leu211Gly
 30 Ala194Gln + Pro195Gly + Gly196Asn + Val197Cys + Asn198Gln
 + Pro204Glu + Thr207Asp + Gly213Gln
 Pro195Gly + Asn198Asp + Gln200Glu + Tyr203Thr + Gly205Asn
 + Leu211Cys + Asn212Ser + Gly213Gln
 Ala194Gly + Pro195Asn + Asn198Glu + Gln200Glu + Thr202Gln
 35 + Gly205Ser + Thr207Pro + Gly213Gln
 Pro195Gly + Asn198Glu + Val199Gln + Gln200Asp + Thr202Gly
 + Pro204Gln + Thr207Pro + Leu211Cys
 Pro195Asn + Gly196Gln + Asn198Glu + Gln200Asp + Thr202Gly
 + Tyr208Gln + Leu211Ser + Thr214Ser
 40 Val197Asn + Asn198Ser + Gln200Glu + Thr202Asn + Tyr203Cys
 + Pro204Ser + Gly205Pro + Tyr208Glu
 Ala194His + Val199His + Tyr203Asn + Tyr208His + Ala209Glu
 + Leu211Asp + Asn212Gln + Gly213Gln
 Gly196Gln + Val197Ser + Gln200Glu + Tyr203Val + Thr207Pro
 45 + Ala209Thr + Leu211Glu + Asn212Ser
 Pro195Gln + Val199Gly + Gln200Asp + Pro204Asn + Gly205Asn
 + Tyr208Ile + Ala209Pro + Leu211Glu
 Pro195Gln + Asn198Ser + Val199Asn + Gln200Asp + Gly205Pro
 + Tyr208Ser + Leu211Glu + Thr214Asn
 50 Ala194His + Pro195Ser + Val197Glu + Val199Cys + Thr202Pro
 + Leu211Glu + Asn212Gln + Thr214Asn
 Ala194Ser + Pro195Gln + Asn198Ser + Gln200Asn + Gly205Gln
 + Leu211Asp + Asn212Gln + Gly213Glu
 Gly196Gln + Val199Gln + Tyr203Gly + Gly205Asn + Ala209His

+ Leu211Asp + Asn212Gln + Gly213Asp
 Asn198Gln + Gln200Ser + Tyr203Leu + Gly205Asn + Thr207Glu
 + Ala209Asp + Leu211Ser + Gly213Asn
 Ala194Ser + Pro195Ser + Val199Gln + Gln200Ser + Gly205Gln
 5 + Ser210Asp + Asn212Glu + Thr214Gln
 Pro195Asn + Tyr203Cys + Pro204Gln + Tyr208Asn + Ala209His
 + Ser210Asp + Asn212Asp + Thr214Gly
 Gly196Asn + Val199Ser + Thr202Gln + Pro204Ser + Thr207Gly
 + Ser210Glu + Leu211Thr + Asn212Asp
 10 Gly196Gln + Val197Cys + Asn198Ser + Pro204Gln + Thr207Asn
 + Ala209Gln + Ser210Asp + Asn212Asp
 Pro195Gly + Gly196Pro + Val197Cys + Asn198Ser + Gln200Asn
 + Tyr208His + Ser210Asp + Asn212Glu
 Pro195Gln + Asn198Ser + Val199Gly + Thr202Pro + Thr207Ser
 15 + Tyr208Ile + Ser210Asp + Asn212Asp
 Ala194Asn + Val197Met + Val199Thr + Ala209Asn + Ser210Asp
 + Leu211Val + Asn212Glu + Gly213Gln
 Ala194Gln + Pro195Asn + Val199Asn + Tyr203Ser + Thr207Asn
 + Ser210Asp + Leu211Gly + Asn212Asp
 20 Val199Cys + Gln200Ser + Thr202Asn + Gly205Asn + Thr207Gly
 + Tyr208Asn + Ser210Glu + Asn212Asp
 Ala194Thr + Val199Cys + Gln200Ser + Gly205Ser + Ser206Glu
 + Tyr208Asp + Leu211Ala + Gly213Asn
 Ala194Pro + Val197Pro + Gln200Ser + Ser206Asp + Thr207Pro
 25 + Tyr208Asp + Ala209Pro + Thr214Gly
 Gly196Gln + Asn198Ser + Val199Met + Thr202Ser + Pro204Asn
 + Ser206Glu + Tyr208Glu + Asn212Gln
 Pro195Asn + Gly196Asn + Val199Ala + Gln200Asn + Ser206Asp
 + Thr207Asn + Tyr208Asp + Ala209Ser
 30 Gly196Asn + Tyr203Ala + Pro204Ser + Ser206Asp + Tyr208Asp
 + Ala209Ser + Asn212Ser + Thr214Gln
 Val197Gly + Asn198Ser + Tyr203Asn + Pro204Gly + Gly205Ser
 + Thr207Pro + Asn212Asp + Thr214Asp
 Ala194Gln + Val197Asp + Asn198Gln + Tyr203His + Ser210Glu
 35 + Leu211Ala + Gly213Ser + Thr214Asn
 Ala194Pro + Val197Glu + Val199His + Gln200Ser + Tyr203His
 + Pro204Asn + Tyr208Thr + Thr214Glu
 Gly196Asn + Asn198Asp + Val199Gln + Gln200Ser + Thr202Ser
 + Pro204Ser + Leu211Cys + Gly213Glu
 40 Asn198Asp + Tyr203Met + Pro204Gly + Thr207Asn + Tyr208Gln
 + Ala209Glu + Asn212Ser + Thr214Ser
 Asn198Glu + Val199Gly + Thr202Gly + Thr207Gln + Tyr208Cys
 + Ala209Asp + Leu211Thr + Asn212Gln
 Ala194His + Val197Asp + Asn198Gln + Gln200Glu + Thr202Asn
 45 + Tyr208Pro + Leu211Ser + Asn212Ser
 Pro195Gly + Gln200Asp + Tyr203Gly + Gly205Asn + Leu211Ser
 + Asn212Glu + Gly213Gln + Thr214Gln
 Ala194Asn + Gly196Ser + Val199Pro + Gln200Glu + Thr207Gly
 + Tyr208Asn + Ala209Thr + Asn212Glu
 50 Ala194Thr + Val199Asn + Gln200Glu + Tyr203Gln + Pro204Gly
 + Ala209His + Asn212Glu + Thr214Ser
 Ala194Asn + Gly196Pro + Val197Ser + Asn198Gln + Tyr203Pro
 + Pro204Asp + Tyr208Asn + Ala209Asp
 Pro195Ser + Val199Cys + Gln200Ser + Pro204Glu + Gly205Ser

+ Tyr208Ala + Ala209Glu + Asn212Gln
 Asn198Gln + Val199His + Thr202Gly + Pro204Glu + Gly205Pro
 + Tyr208Ala + Ala209Glu + Asn212Gln
 Gly196Ser + Asn198Ser + Val199Gly + Gln200Ser + Gly205Ser
 5 + Tyr208Asp + Leu211Asp + Thr214Ser
 Pro195Gln + Gly196Asn + Val197Gly + Gln200Asn + Pro204Asn
 + Thr207Gly + Ala209Asp + Asn212Glu
 Ala194Ser + Gln200Ser + Gly205Ser + Ala209Asp + Leu211Gly
 + Asn212Asp + Gly213Gln + Thr214Asn
 10 Ala194Gln + Pro195Gln + Gly196Pro + Tyr203Leu + Pro204Ser
 + Ser206Asp + Ala209Glu + Leu211Pro
 Thr202Asn + Tyr203Ala + Pro204Ser + Ser206Asp + Tyr208Cys
 + Ala209Glu + Leu211Cys + Asn212Ser
 Gly196Ser + Val199His + Gln200Asn + Gly205Asn + Ser206Glu
 15 + Ala209Asp + Leu211His + Asn212Ser
 Ala194Asn + Val197Ala + Gln200Ser + Ser206Glu + Thr207Pro
 + Ala209Glu + Asn212Gln + Gly213Asn
 Pro195Gln + Val197Met + Val199Thr + Gln200Ser + Tyr203Ala
 + Ala209Ser + Ser210Glu + Gly213Glu
 20 Asn198Ser + Val199Asn + Ala209Pro + Ser210Glu + Leu211Gly
 + Asn212Ser + Gly213Asp + Thr214Gly
 Ala194Gly + Asn198Gln + Tyr203Ala + Gly205Asp + Tyr208Gln
 + Ala209Asp + Leu211Ala + Asn212Gln
 Ala194Gly + Gly196Gln + Thr202Gln + Tyr203Thr + Thr207Asp
 25 + Tyr208Thr + Ser210Glu + Asn212Ser
 Ala194Pro + Val197Thr + Tyr203Pro + Pro204Ser + Thr207Asp
 + Ser210Asp + Leu211Pro + Thr214Ser
 Pro195Asn + Val199Ala + Thr202Ser + Gly205Gln + Thr207Asp
 + Ala209His + Ser210Glu + Gly213Asn
 30 Pro195Gly + Gly196Ser + Val197Pro + Pro204Gly + Thr207Glu
 + Tyr208Gln + Ala209His + Ser210Asp
 Ala194Asn + Pro195Asn + Asn198Ser + Val199His + Thr207Asp
 + Tyr208Val + Ala209Pro + Ser210Glu
 Ala194Gly + Gly196Ser + Asn198Asp + Thr207Asn + Ala209Gln
 35 + Leu211Pro + Gly213Gln + Thr214Asp
 Ala194Gly + Pro195Ser + Val197His + Asn198Asp + Gln200Asn
 + Pro204Ser + Asn212Ser + Thr214Asp
 Val199Asn + Gln200Glu + Pro204Gly + Gly205Asn + Tyr208Ser
 + Leu211Ala + Asn212Ser + Gly213Glu
 40 Ala194Gln + Pro195Ser + Gly196Asn + Asn198Gln + Gln200Glu
 + Tyr203Cys + Leu211Ser + Gly213Glu
 Ala194Ser + Gly196Asn + Val197Thr + Asn198Gln + Gln200Glu
 + Thr207Asn + Tyr208His + Gly213Asp
 Ala194Gln + Val197Gln + Asn198Asp + Gln200Asn + Gly205Gln
 45 + Tyr208Asp + Leu211Gly + Thr214Ser
 Ala194Ser + Asn198Ser + Thr202Pro + Pro204Asp + Gly205Gln
 + Thr207Asn + Ser210Asp + Asn212Ser
 Pro195Gln + Gly196Asn + Pro204Glu + Gly205Asn + Thr207Asn
 + Tyr208Ser + Ala209Pro + Ser210Asp
 50 Ala194Thr + Gly196Pro + Val199Pro + Gln200Asn + Pro204Glu
 + Ala209Thr + Ser210Asp + Leu211Ala
 Ala194Ser + Gly196Gln + Val199Thr + Pro204Glu + Tyr208Ile
 + Ala209Gln + Ser210Asp + Thr214Gly
 Ala194His + Val197Ser + Val199Ser + Gln200Ser + Pro204Glu

+ Thr207Gly + Ala209Pro + Ser210Asp
 Ala194Gln + Val197Ala + Asn198Ser + Pro204Asp + Tyr206Cys
 + Ala209Gly + Ser210Asp + Asn212Ser
 Gly196Ser + Val197Thr + Asn198Ser + Gln200Glu + Thr202Pro
 5 + Pro204Glu + Ala209Thr + Gly213Ser
 Pro195Asn + Val197Pro + Val199Gly + Gln200Asp + Pro204Glu
 + Thr207Gly + Leu211Thr + Gly213Ser
 Ala194Gln + Val197Asn + Gln200Ser + Thr202Gln + Thr207Glu
 + Ala209Gly + Leu211Glu + Gly213Asn
 10 Ala194Ser + Gly196Ser + Val197Ser + Asn198Gln + Gly205Gln
 + Ser210Glu + Asn212Ser + Thr214Asp
 Gly196Ser + Val199Cys + Gln200Ser + Thr207Pro + Tyr208Pro
 + Ala209Gly + Ser210Asp + Thr214Asp
 Val197Cys + Val199Gly + Tyr203Gly + Tyr208Met + Ala209Ser
 15 + Ser210Glu + Leu211Ala + Thr214Glu
 Ala194Pro + Pro195Ser + Gly196Ser + Val199Asn + Thr202Gly
 + Ser210Asp + Asn212Gln + Thr214Glu
 Ala194Asn + Gly196Asn + Gln200Ser + Pro204Asn + Gly205Ser
 + Ala209Ser + Ser210Asp + Thr214Asp
 20 Ala194His + Val197Cys + Tyr208Ile + Ser210Glu + Leu211Gly
 + Asn212Ser + Gly213Asn + Thr214Asp
 Gly196Gln + Gln200Asn + Thr202Pro + Tyr203Cys + Gly205Gln
 + Tyr208Ser + Ser210Glu + Thr214Asp
 Asn198Gln + Val199Pro + Gln200Glu + Thr202Pro + Pro204Ser
 25 + Ser206Glu + Tyr208Gln + Thr214Asn
 Pro195Gly + Gln200Asp + Tyr203Val + Ser206Asp + Tyr208Thr
 + Leu211Gly + Asn212Gln + Gly213Asn
 Gly196Gln + Gln200Glu + Thr202Gln + Tyr203Val + Ser206Glu
 + Tyr208Val + Ala209Asn + Leu211Gly
 30 Pro195Gly + Gln200Glu + Thr202Pro + Gly205Ser + Ser206Glu
 + Ala209Gln + Leu211His + Asn212Gln
 Asn198Gln + Gln200Glu + Pro204Gly + Gly205Gln + Ser206Asp
 + Tyr208Met + Asn212Ser + Thr214Asn
 Ala194Pro + Pro195Gln + Gly196Ser + Val197His + Gln200Glu
 35 + Gly205Ser + Ser206Glu + Leu211Ser
 Ala194Gln + Gln200Asp + Tyr203Gln + Pro204Asn + Ser206Glu
 + Tyr208Ile + Ala209Gly + Gly213Asn
 Ala194Gln + Pro195Gln + Val197His + Gln200Glu + Pro204Ser
 + Ser206Asp + Tyr208Gln + Ala209Asn
 40 Pro195Gln + Val197His + Val199Asn + Gln200Asp + Thr202Pro
 + Ser206Glu + Leu211Thr + Thr214Pro
 Pro195Gly + Asn198Gln + Val199Cys + Gln200Asp + Thr202Gly
 + Ser206Glu + Tyr208Cys + Gly213Ser
 Ala194Gly + Pro195Asn + Gly196Asn + Pro204Asp + Thr207Ser
 45 + Leu211Glu + Asn212Gln + Thr214Asn

TABLE 31

Loop 6 - Nonuple Mutation Variants

50 Ala194Gly + Pro195Ser + Val197Cys + Val199Asn + Gln200Asp
 + Tyr203Pro + Pro204Ser + Gly205Ser + Leu211Gln
 Ala194Pro + Gln200Asn + Thr202Asn + Tyr203Asn + Pro204Ser
 + Tyr208Asn + Ala209Asn + Ser210Asp + Thr214Gln

Pro195Gly + Val199Ala + Gln200Ser + Thr202Gly + Gly205Pro
+ Ser206Glu + Ala209His + Leu211Ala + Gly213Asn
Pro195Gln + Gly196Gln + Val197Thr + Val199His + Thr202Gln
+ Tyr203Gly + Pro204Gly + Gly205Glu + Gly213Gln
5 Pro195Gly + Val197Gly + Val199Asn + Pro204Asn + Ser206Asp
+ Thr207Ser + Tyr208Gln + Ala209Gly + Thr214Asn
Ala194Thr + Val197Asn + Val199Pro + Gln200Asp + Thr202Ser
+ Tyr203Asn + Thr207Asn + Tyr208Leu + Ala209Gly
Pro195Asn + Gly196Asn + Asn198Gln + Tyr203Gln + Thr207Ser
10 + Ala209Thr + Leu211Ala + Asn212Asp + Thr214Asn
Ala194Gln + Pro195Gly + Gly196Pro + Val197Gly + Gln200Asp
+ Thr202Ser + Pro204Gly + Tyr208Thr + Thr214Gln
Gly196Asn + Val199Gly + Tyr203Ser + Pro204Ser + Tyr208Gln
+ Ala209His + Asn212Ser + Gly213Asp + Thr214Gln
15 Val197His + Gln200Ser + Thr202Asn + Pro204Ser + Thr207Pro
+ Tyr208Gly + Ala209His + Ser210Glu + Leu211Ala
Pro195Ser + Val197His + Gln200Glu + Thr202Gln + Pro204Ser
+ Tyr208Val + Ala209His + Leu211Thr + Thr214Pro
Pro195Gly + Gly196Pro + Val199Thr + Thr202Pro + Tyr203Ile
20 + Thr207Gly + Ala209Pro + Ser210Asp + Asn212Gln
Ala194Gly + Pro195Gln + Val197Asp + Tyr203Cys + Tyr208Val
+ Ala209Gln + Leu211Gly + Asn212Gln + Gly213Gln
Gly196Asn + Asn198Gln + Thr202Gly + Thr207Asp + Tyr208Gly
+ Ala209Ser + Leu211Thr + Asn212Ser + Thr214Pro
25 Ala194Pro + Gly196Asn + Val197Met + Gln200Glu + Tyr203Gln
+ Gly205Asn + Tyr208Asn + Ala209Thr + Thr214Gln
Ala194Pro + Gly196Gln + Val197Asn + Gly205Ser + Ser206Asp
+ Thr207Asn + Ala209Ser + Leu211Cys + Thr214Pro
Gly196Gln + Val197Thr + Gln200Ser + Tyr203Asn + Pro204Asn
30 + Gly205Pro + Tyr208Ser + Ser210Glu + Asn212Ser
Ala194Thr + Pro195Ser + Gly196Pro + Val197Cys + Gln200Glu
+ Pro204Ser + Gly205Asn + Ala209His + Leu211Pro
Pro195Gln + Gly196Asn + Asn198Gln + Val199Gln + Gln200Asp
+ Pro204Ser + Gly205Asn + Thr207Ser + Tyr208Ser
35 Ala194His + Val197Asn + Tyr203Gly + Pro204Gln + Thr207Gly
+ Ala209Gln + Leu211His + Asn212Gln + Gly213Gln
Ala194Ser + Pro195Gln + Val197Met + Val199His + Thr207Pro
+ Tyr208Ala + Asn212Gln + Gly213Glu + Thr214Asn
Gly196Pro + Val197His + Asn198Gln + Gln200Glu + Tyr203Ser
40 + Gly205Pro + Thr207Ser + Leu211Thr + Gly213Asn
Gly196Ser + Val197Asn + Val199Thr + Thr202Gly + Tyr203Asn
+ Pro204Asn + Ala209Gln + Leu211Pro + Thr214Asp
Ala194Thr + Pro195Ser + Val197Asn + Tyr203Met + Tyr208Ala
+ Ala209Ser + Asn212Gln + Gly213Asp + Thr214Asp
45 Ala194Asn + Gly196Gln + Val197Thr + Val199Ala + Gly205Asn
+ Ala209Pro + Leu211Asn + Gly213Glu + Thr214Asp
Pro195Asn + Val199Met + Gln200Asn + Thr202Asn + Tyr203Cys
+ Ala209Ser + Leu211Gln + Gly213Asp + Thr214Glu
Pro195Asn + Val197Met + Asn198Ser + Val199Asn + Gln200Asn
50 + Tyr208Gln + Leu211His + Gly213Glu + Thr214Asp
Val197His + Val199Ala + Gln200Ser + Pro204Ser + Ala209Glu
+ Ser210Glu + Asn212Gln + Gly213Pro + Thr214Ser
Gly196Gln + Val197Asn + Asn198Gln + Thr202Gly + Gly205Gln
+ Ala209Asp + Ser210Glu + Leu211Met + Thr214Gly

Vall197Cys + Asn198Ser + Vall199Gln + Tyr203Gly + Pro204Gln
+ Ala209Glu + Ser210Glu + Gly213Pro + Thr214Gly
Pro195Asn + Vall199His + Gln200Ser + Pro204Gln + Gly205Gln
+ Ala209Glu + Ser210Asp + Leu211Gln + Asn212Gln
5 Vall197Asp + Asn198Glu + Vall199Met + Thr202Gln + Pro204Ser
+ Gly205Gln + Thr207Gln + Tyr208His + Asn212Ser
Ala194Thr + Vall197Glu + Asn198Asp + Vall199His + Tyr203Asn
+ Tyr208His + Ala209Ser + Gly213Ser + Thr214Asn
Vall197Cys + Asn198Ser + Vall199Pro + Gln200Ser + Tyr203Ala
10 + Tyr208Asn + Asn212Asp + Gly213Glu + Thr214Ser
Gly196Asn + Vall197Met + Asn198Ser + Thr202Gly + Pro204Gln
+ Ala209Ser + Leu211His + Asn212Asp + Gly213Asp
Ala194Thr + Pro195Ser + Gln200Asn + Thr202Asn + Tyr203Gln
+ Tyr208Ser + Leu211Ala + Asn212Asp + Gly213Asp
15 Pro195Gly + Asn198Ser + Vall199Pro + Gly205Asp + Ser206Asp
+ Thr207Pro + Tyr208Ala + Asn212Ser + Gly213Ser
Pro195Gln + Asn198Ser + Gln200Asn + Thr202Ser + Tyr203Met
+ Gly205Asp + Ser206Glu + Thr207Pro + Thr214Ser
Gly196Ser + Vall199Thr + Gln200Asn + Tyr203Ala + Gly205Asp
20 + Ser206Asp + Tyr208Leu + Ala209Thr + Gly213Pro
Ala194Pro + Gly196Ser + Vall197Asn + Vall199His + Gln200Asn
+ Gly205Glu + Ser206Glu + Asn212Gln + Thr214Gln
Ala194Thr + Vall199Ser + Thr202Asn + Gly205Glu + Ser206Asp
+ Ala209Pro + Leu211Pro + Asn212Gln + Gly213Gln
25 Asn198Ser + Thr202Ser + Tyr203Ser + Pro204Gly + Gly205Asn
+ Ser206Asp + Thr207Glu + Ala209Pro + Thr214Ser
Pro195Asn + Gly196Asn + Vall197Pro + Vall199Ser + Thr202Ser
+ Ser206Glu + Thr207Glu + Leu211Ile + Gly213Ser
Thr202Ser + Tyr203Thr + Thr207Asp + Tyr208Glu + Ala209Pro
30 + Leu211Val + Asn212Ser + Gly213Ser + Thr214Asn
Vall199Pro + Gln200Ser + Thr202Ser + Thr207Asp + Tyr208Asp
+ Ala209Gly + Leu211Met + Asn212Ser + Thr214Pro
Ala194Gln + Pro195Gly + Vall197Ala + Gln200Glu + Tyr203Thr
+ Gly205Ser + Ala209Pro + Ser210Asp + Thr214Asn
35 Ala194Pro + Pro195Ser + Vall199Met + Gln200Glu + Thr202Gly
+ Pro204Gln + Gly205Asn + Tyr208Gln + Ser210Asp
Ala194Gln + Vall199Pro + Gln200Asp + Pro204Gly + Gly205Gln
+ Thr207Pro + Tyr208Asn + Ala209Gln + Ser210Asp
Ala194Pro + Gly196Pro + Asn198Gln + Gln200Asp + Pro204Gly
40 + Gly205Asn + Tyr208Ile + Ser210Asp + Asn212Ser
Pro195Ser + Asn198Ser + Vall199Ala + Gln200Glu + Tyr203Thr
+ Gly205Gln + Tyr208Met + Ser210Glu + Gly213Pro
Pro195Asn + Asn198Ser + Gln200Asp + Thr202Gln + Tyr203Ala
+ Gly205Pro + Ser210Asp + Leu211Ser + Gly213Ser
45 Pro195Asn + Gly196Asn + Vall197Ala + Asn198Ser + Gln200Asp
+ Tyr203Gln + Pro204Asn + Ala209Ser + Ser210Asp
Pro195Ser + Vall197Pro + Asn198Gln + Vall199Pro + Gln200Glu
+ Thr202Gln + Thr207Asn + Ala209His + Ser210Glu
Pro195Ser + Gly196Asn + Asn198Gln + Gln200Glu + Thr202Ser
50 + Pro204Gly + Thr207Asn + Ser210Glu + Thr214Asn
Ala194Ser + Pro195Ser + Vall197His + Vall199Thr + Gln200Glu
+ Gly205Gln + Thr207Gly + Ser210Glu + Gly213Pro
Pro195Asn + Vall197Asp + Asn198Ser + Vall199Asn + Thr207Pro
+ Tyr208Ala + Leu211Val + Asn212Glu + Gly213Ser

Pro195Asn + Gly196Asn + Val197Gln + Asn198Glu + Val199Thr
+ Tyr203Asn + Thr207Pro + Ser210Glu + Gly213Gln
Val197Cys + Asn198Asp + Val199Ser + Tyr203Gln + Gly205Ser
+ Thr207Ser + Tyr208Leu + Ser210Asp + Leu211Gly
5 Ala194Pro + Gly196Gln + Val197Gly + Asn198Glu + Gln200Ser
+ Tyr203Thr + Pro204Ser + Ala209His + Ser210Glu
Gly196Ser + Val197His + Asn198Glu + Thr202Pro + Tyr203Ile
+ Thr207Asn + Tyr208Val + Ser210Glu + Thr214Ser
Gly196Asn + Val197Thr + Asn198Asp + Val199Ala + Pro204Asn
10 + Ser210Asp + Leu211Val + Gly213Gln + Thr214Pro
Gly196Ser + Asn198Glu + Thr202Asn + Gly205Ser + Thr207Gln
+ Tyr208Ile + Ser210Glu + Leu211Ser + Asn212Ser
Ala194Asn + Gly196Pro + Asn198Asp + Thr202Gly + Tyr208Ser
+ Ala209Pro + Ser210Glu + Leu211Ala + Thr214Asn
15 Ala194His + Asn198Glu + Val199Gly + Gln200Asn + Gly205Asn
+ Ser210Glu + Leu211His + Asn212Gln + Thr214Ser
Ala194Gly + Asn198Glu + Gln200Asn + Thr202Pro + Tyr203Cys
+ Thr207Gln + Tyr208Met + Ser210Asp + Asn212Gln
Pro195Gly + Gly196Gln + Asn198Glu + Gln200Ser + Pro204Gln
20 + Tyr208Leu + Ala209Thr + Ser210Glu + Leu211Ile
Ala194Pro + Pro195Gln + Val197His + Asn198Glu + Thr202Gln
+ Gly205Pro + Thr207Asn + Tyr208Val + Leu211Asp
Pro195Gln + Asn198Glu + Thr202Ser + Tyr203Gly + Pro204Ser
+ Thr207Gln + Ala209Pro + Leu211Asp + Gly213Asn
25 Val199Asn + Gln200Asp + Thr202Gln + Tyr203Gly + Pro204Asn
+ Thr207Gln + Tyr208Ala + Ala209Glu + Asn212Ser
Gly196Pro + Val197Thr + Pro204Asp + Ser206Glu + Ala209Gln
+ Leu211Gln + Asn212Ser + Gly213Ser + Thr214Pro
Gly196Pro + Asn198Ser + Val199Thr + Pro204Glu + Ser206Asp
30 + Thr207Gln + Ala209Gly + Asn212Ser + Thr214Gly
Ala194Asn + Val197Gly + Gln200Ser + Thr202Ser + Pro204Asp
+ Ser206Asp + Tyr208Gln + Ala209Gln + Leu211Gly
Ala194Pro + Thr202Gln + Tyr203Asn + Pro204Asp + Ser206Glu
+ Tyr208Gly + Ala209Ser + Gly213Pro + Thr214Pro
35 Ala194Asn + Pro195Gln + Val197Thr + Asn198Ser + Pro204Asp
+ Gly205Ser + Ser206Asp + Asn212Ser + Thr214Asn
Pro195Gly + Gln200Ser + Thr202Gln + Tyr203Pro + Pro204Asp
+ Gly205Asn + Ser206Glu + Thr207Asn + Leu211His
Ala194His + Gly196Asn + Val197Met + Asn198Ser + Pro204Asp
40 + Ser206Asp + Leu211Asn + Asn212Ser + Thr214Gln
Asn198Gln + Val199Cys + Gln200Ser + Thr202Gln + Pro204Asp
+ Gly205Gln + Ser206Asp + Tyr208Leu + Thr214Pro
Ala194His + Pro195Ser + Gly196Pro + Asn198Gln + Pro204Glu
+ Ser206Asp + Thr207Pro + Tyr208His + Ala209Asn
45 Ala194Ser + Asn198Asp + Gln200Ser + Thr202Gly + Thr207Pro
+ Tyr208Asn + Ala209Gln + Leu211Ser + Asn212Glu
Gly196Asn + Asn198Gln + Gln200Asn + Tyr203Thr + Pro204Ser
+ Gly205Asp + Thr207Glu + Ala209Ser + Thr214Asn
Val197His + Asn198Gln + Val199Met + Gln200Ser + Pro204Glu
50 + Gly205Ser + Thr207Glu + Tyr208Val + Thr214Gly
Val197Asn + Asn198Asp + Val199Ala + Gln200Glu + Tyr203Cys
+ Pro204Gly + Gly205Asn + Thr207Gln + Gly213Asn
Pro195Asn + Gly196Gln + Asn198Asp + Val199Pro + Gln200Glu
+ Tyr203Val + Gly205Asn + Tyr208Cys + Ala209Pro

Pro195Gly + Gly196Pro + Val197Asp + Thr202Ser + Pro204Gln
 + Thr207Gly + Tyr208Ile + Asn212Gln + Gly213Glu
 Ala194Pro + Val197Glu + Tyr203His + Gly205Pro + Thr207Gly
 + Ala209Asn + Leu211His + Gly213Asp + Thr214Gly
 5 Pro195Gln + Val197Glu + Asn198Gln + Val199Ala + Pro204Ser
 + Gly205Gln + Ala209Ser + Gly213Glu + Thr214Ser
 Pro195Asn + Val197Asp + Asn198Gln + Val199Ser + Gln200Ser
 + Thr207Ser + Tyr208Ile + Asn212Ser + Gly213Asp
 Gly196Pro + Val197Glu + Asn198Gln + Val199Asn + Pro204Gly
 10 + Thr207Pro + Leu211His + Gly213Asp + Thr214Asn
 Ala194Ser + Asn198Gln + Thr202Pro + Tyr203Met + Pro204Ser
 + Thr207Gln + Ala209Asp + Leu211Glu + Thr214Gln
 Gly196Pro + Val197Pro + Thr202Asn + Tyr203Cys + Tyr208Gln
 + Ser210Asp + Asn212Asp + Gly213Pro + Thr214Ser
 15 Pro195Gln + Tyr203Thr + Gly205Gln + Ala209Gln + Ser210Asp
 + Leu211Asn + Asn212Glu + Gly213Asn + Thr214Gln
 Ala194Gly + Pro195Ser + Val197His + Thr202Gln + Pro204Gly
 + Ser210Asp + Leu211His + Asn212Glu + Thr214Gly
 Pro195Asn + Gly196Asn + Val197Asn + Thr202Ser + Tyr203Val
 20 + Gly205Ser + Ser210Asp + Asn212Glu + Gly213Pro
 Gln200Ser + Thr202Gly + Tyr203Leu + Thr207Pro + Tyr208Pro
 + Ser210Asp + Leu211Pro + Asn212Glu + Thr214Gly
 Ala194Gln + Gly196Ser + Val197Cys + Val199Met + Tyr203Leu
 + Ala209Thr + Ser210Asp + Asn212Glu + Thr214Ser
 25 Val197Met + Val199Ala + Gln200Asn + Tyr203Thr + Thr207Gln
 + Tyr208Glu + Ser210Glu + Asn212Ser + Thr214Gly
 Gly196Ser + Val197Ala + Val199Ser + Thr202Gly + Tyr203Cys
 + Gly205Asn + Ser206Glu + Tyr208Asp + Leu211Ile
 Ala194Gly + Pro195Ser + Val199His + Thr202Asn + Gly205Gln
 30 + Ser206Asp + Tyr208Glu + Asn212Ser + Thr214Pro
 Gly196Pro + Val199Gln + Thr202Ser + Gly205Pro + Ser206Asp
 + Thr207Gln + Tyr208Glu + Leu211His + Asn212Ser
 Val197His + Asn198Ser + Gly205Ser + Thr207Pro + Tyr208Val
 + Leu211Val + Asn212Glu + Gly213Ser + Thr214Glu
 35 Pro195Ser + Gly196Pro + Val199Thr + Tyr203Ser + Tyr208Gly
 + Ala209Asn + Asn212Glu + Gly213Ser + Thr214Glu
 Pro195Asn + Asn198Gln + Gln200Asn + Thr202Asn + Thr207Asn
 + Tyr208Gln + Asn212Glu + Gly213Ser + Thr214Glu
 Ala194Asn + Val199Ser + Thr202Gly + Pro204Asn + Gly205Ser
 40 + Ala209Asn + Leu211Asn + Asn212Asp + Thr214Glu
 Ala194Ser + Gly196Gln + Pro204Asp + Gly205Pro + Thr207Pro
 + Tyr208Glu + Leu211Ile + Gly213Asn + Thr214Ser
 Pro195Ser + Val197Asp + Asn198Gln + Gln200Asn + Tyr203Pro
 + Gly205Asn + Ser210Asp + Asn212Ser + Thr214Asn
 45 Ala194His + Gly196Ser + Val197Asp + Asn198Ser + Gln200Asn
 + Thr202Ser + Gly205Gln + Ser210Glu + Asn212Ser
 Ala194Thr + Val197Glu + Thr202Gln + Pro204Gln + Tyr208Gly
 + Ala209Thr + Ser210Glu + Asn212Ser + Thr214Gln
 Gly196Ser + Val197Asp + Val199Pro + Tyr203Cys + Pro204Ser
 50 + Thr207Asn + Tyr208Asn + Ser210Asp + Asn212Ser
 Ala194Pro + Pro195Ser + Gly196Gln + Val197Asp + Val199Met
 + Gln200Asn + Leu211Met + Gly213Pro + Thr214Asp
 Pro195Asn + Gly196Gln + Asn198Gln + Val199Ala + Gln200Ser
 + Tyr203Pro + Gly205Glu + Thr207Asn + Tyr208Asp

Gly196Pro + Asn198Ser + Val199Asn + Thr202Gly + Pro204Gln
 + Gly205Asp + Thr207Gln + Tyr208Asp + Thr214Asn
 Val197Ser + Asn198Glu + Gln200Asn + Tyr203Gln + Pro204Asn
 + Gly205Pro + Thr207Gly + Ala209Thr + Gly213Glu
 5 Alal94Thr + Gly196Gln + Val197His + Asn198Asp + Val199Ser
 + Tyr203Pro + Tyr208Cys + Gly213Asp + Thr214Pro
 Asn198Asp + Gln200Ser + Tyr203Gln + Pro204Ser + Gly205Asn
 + Thr207Asn + Ala209Glu + Leu211Gln + Asn212Ser
 Pro195Gly + Gly196Asn + Asn198Glu + Thr202Gln + Tyr203Ala
 10 + Pro204Ser + Thr207Pro + Ala209Glu + Gly213Gln
 Alal94Pro + Asn198Glu + Val199Thr + Pro204Gly + Thr207Gly
 + Tyr208Ile + Ala209Asp + Leu211Met + Asn212Ser
 Alal94Ser + Val197Glu + Val199Thr + Gln200Asp + Tyr203Gly
 + Gly205Ser + Tyr208His + Ala209Thr + Asn212Ser
 15 Gly196Gln + Val197Glu + Val199Pro + Gln200Asp + Gly205Gln
 + Thr207Ser + Ala209Thr + Leu211Pro + Thr214Gly
 Val197Gly + Gln200Glu + Thr202Gly + Tyr203Leu + Gly205Gln
 + Thr207Gly + Tyr208Leu + Ala209Asn + Asn212Asp
 Pro195Ser + Gly196Asn + Asn198Ser + Val199His + Gln200Glu
 20 + Tyr203Pro + Ala209Ser + Asn212Asp + Thr214Asn
 Asn198Ser + Val199Met + Gln200Glu + Thr202Ser + Tyr203Ile
 + Gly205Pro + Ala209Pro + Asn212Glu + Gly213Gln
 Gly196Pro + Val197Ser + Val199Pro + Gln200Glu + Ala209Gly
 + Leu211Gln + Asn212Asp + Gly213Pro + Thr214Asn
 25 Alal94Gln + Gly196Ser + Val197Pro + Thr202Pro + Pro204Asp
 + Tyr208Gly + Ala209Glu + Gly213Asn + Thr214Pro
 Alal94Pro + Val197Ser + Val199His + Gln200Asn + Pro204Gly
 + Ser206Glu + Thr207Asn + Tyr208Leu + Ala209Glu
 Gly196Asn + Thr202Asn + Pro204Asn + Gly205Pro + Ser206Glu
 30 + Tyr208Asn + Ala209Asp + Leu211Met + Thr214Gln
 Pro195Gly + Asn198Gln + Val199Ser + Gln200Ser + Tyr203Thr
 + Gly205Pro + Ser206Glu + Ala209Glu + Thr214Asn
 Alal94Thr + Val197Ala + Thr202Ser + Tyr203Pro + Gly205Asn
 + Ser206Glu + Ala209Glu + Leu211Gln + Thr214Asn
 35 Pro195Ser + Val197Ala + Thr202Asn + Pro204Gly + Ser206Asp
 + Thr207Asn + Ala209Glu + Asn212Ser + Thr214Ser
 Alal94Thr + Val199Asn + Thr202Pro + Tyr203Ile + Pro204Asn
 + Ser206Asp + Thr207Asn + Ala209Glu + Thr214Asn
 Alal94Ser + Pro195Asn + Val197Gly + Val199Gly + Gln200Glu
 40 + Thr202Gln + Pro204Asn + Thr207Asp + Leu211Gln
 Alal94Gly + Val197His + Gln200Ser + Pro204Asn + Thr207Ser
 + Ser210Glu + Leu211Gly + Gly213Glu + Thr214Asn
 Alal94Gln + Gly196Gln + Val197Met + Val199His + Thr202Pro
 + Gly205Asn + Ala209Ser + Ser210Glu + Gly213Glu
 45 Pro195Asn + Val197Thr + Val199Ala + Gln200Asn + Tyr203Asn
 + Thr207Gly + Ser210Asp + Asn212Gln + Gly213Glu
 Alal94His + Val199Pro + Gln200Asn + Thr202Pro + Tyr203Asn
 + Gly205Glu + Ala209Glu + Asn212Gln + Thr214Asn
 Gly196Pro + Asn198Gln + Gln200Asn + Tyr203Gln + Pro204Gln
 50 + Gly205Asp + Ala209Glu + Asn212Gln + Thr214Gln
 Pro195Gln + Asn198Gln + Val199Ala + Gln200Asn + Thr207Glu
 + Tyr208Leu + Ala209Ser + Ser210Asp + Gly213Pro
 Pro195Gly + Gly196Gln + Val199Ser + Gln200Asn + Pro204Ser
 + Gly205Ser + Thr207Glu + Ser210Glu + Thr214Pro

Gly196Gln + Gln200Ser + Thr202Gly + Tyr203Ile + Thr207Asp
+ Tyr208Ile + Ser210Asp + Leu211Asn + Asn212Ser
Ala194His + Gly196Gln + Val197Gly + Thr207Glu + Tyr208Val
+ Ala209Gln + Ser210Asp + Leu211His + Gly213Ser
5 Ala194Gln + Asn198Asp + Val199Ser + Gln200Ser + Tyr203Ile
+ Gly205Asn + Thr207Asn + Asn212Gln + Thr214Asp
Val197Pro + Asn198Glu + Val199Thr + Gln200Ser + Pro204Asn
+ Gly205Pro + Leu211Cys + Asn212Ser + Thr214Asp
Ala194Ser + Val199Thr + Gln200Glu + Tyr203Cys + Tyr208Gly
10 + Ala209His + Leu211Gly + Asn212Ser + Gly213Glu
Gly196Gln + Asn198Gln + Val199Met + Gln200Asp + Pro204Gln
+ Tyr208Pro + Asn212Gln + Gly213Asp + Thr214Gln
Val197Asp + Val199Gln + Gln200Ser + Thr202Pro + Thr207Gln
+ Ala209Glu + Leu211Gly + Asn212Ser + Gly213Gln
15 Ala194Ser + Gly196Pro + Val197Glu + Asn198Ser + Val199Met
+ Pro204Gly + Thr207Gln + Ala209Glu + Gly213Gln
Val197Asp + Asn198Ser + Pro204Gln + Gly205Gln + Thr207Gly
+ Tyr208Met + Ala209Glu + Asn212Gln + Thr214Gln
Ala194Ser + Val197Glu + Asn198Gln + Tyr203Asn + Gly205Asn
20 + Ala209Glu + Asn212Gln + Gly213Ser + Thr214Pro
Pro195Gly + Val197Ser + Asn198Ser + Tyr203Leu + Pro204Glu
+ Ser210Asp + Leu211Ser + Asn212Ser + Thr214Gln
Ala194Asn + Pro195Gln + Asn198Gln + Val199Asn + Gln200Asn
+ Pro204Asp + Thr207Pro + Ser210Glu + Gly213Gln
25 Ala194Pro + Val197Ser + Asn198Ser + Thr202Pro + Tyr203Val
+ Pro204Glu + Ser210Asp + Asn212Ser + Thr214Asn
Ala194Gln + Pro195Ser + Gly196Pro + Val199Ser + Pro204Asp
+ Tyr208Cys + Ala209Thr + Ser210Glu + Gly213Asn
Pro195Ser + Tyr203Pro + Pro204Asp + Gly205Pro + Thr207Gln
30 + Ala209Gly + Ser210Asp + Leu211Asn + Thr214Asn
Gly196Ser + Asn198Ser + Thr202Pro + Pro204Asp + Tyr208Val
+ Ala209Gln + Ser210Asp + Leu211Asn + Asn212Gln
Gly196Ser + Val199Met + Tyr203Ala + Pro204Glu + Gly205Ser
+ Thr207Ser + Tyr208Leu + Ala209Gln + Ser210Asp
35 Pro195Gly + Val197Pro + Thr202Asn + Pro204Glu + Gly205Ser
+ Thr207Asn + Tyr208Pro + Ser210Glu + Asn212Ser
Ala194Asn + Gly196Ser + Asn198Ser + Val199Met + Gln200Asn
+ Thr202Gly + Thr207Gln + Ala209Asp + Gly213Asp
Ala194Gln + Pro195Gln + Thr202Ser + Pro204Asn + Ala209Thr
40 + Ser210Glu + Leu211Asn + Gly213Gln + Thr214Glu
Gly196Gln + Val197Pro + Asn198Gln + Val199Gly + Ala209Pro
+ Ser210Asp + Leu211Cys + Asn212Ser + Thr214Glu
Ala194Asn + Pro195Gly + Asn198Gln + Val199His + Tyr203Pro
+ Thr207Gly + Tyr208Met + Ser210Asp + Thr214Asp
45 Ala194Pro + Pro195Ser + Gly196Asn + Thr202Gly + Pro204Ser
+ Ala209His + Ser210Glu + Leu211Ser + Thr214Asp
Ala194Thr + Gly196Pro + Asn198Ser + Thr207Asn + Tyr208Ile
+ Ser210Asp + Leu211Val + Gly213Gln + Thr214Glu
Ala194Gly + Pro195Ser + Asn198Ser + Thr202Ser + Gly205Ser
50 + Ala209Gln + Ser210Asp + Asn212Ser + Thr214Asp
Ala194Ser + Pro195Gly + Gly196Ser + Val199Ala + Tyr203Gln
+ Pro204Gln + Thr207Ser + Ser210Glu + Thr214Glu
Gly196Ser + Gln200Asn + Thr202Pro + Tyr203Leu + Thr207Gln
+ Ser210Asp + Leu211Ala + Gly213Pro + Thr214Asp

Ala194Gln + Asn198Ser + Val199Thr + Gln200Ser + Tyr203Thr
 + Ala209Pro + Ser210Asp + Leu211Asn + Thr214Glu
 Pro195Gln + Gly196Gln + Tyr203Cys + Pro204Ser + Gly205Pro
 + Tyr208His + Ala209Thr + Ser210Asp + Thr214Glu
 5 Gly196Gln + Asn198Ser + Val199Thr + Gln200Ser + Thr202Ser
 + Thr207Ser + Ala209His + Ser210Glu + Thr214Glu
 Pro195Asn + Gly196Pro + Asn198Gln + Tyr203Ala + Thr207Ser
 + Ala209Pro + Ser210Asp + Leu211Thr + Thr214Asp
 Ala194Ser + Pro195Asn + Val199Pro + Pro204Asn + Gly205Gln
 10 + Thr207Gln + Ser210Glu + Gly213Ser + Thr214Asp
 Gly196Ser + Val197Asn + Thr202Gln + Tyr203Ser + Pro204Ser
 + Gly205Ser + Ser210Glu + Leu211Cys + Thr214Asp
 Val197Asn + Gln200Asp + Tyr203Cys + Pro204Asn + Gly205Asn
 + Ser206Asp + Thr207Ser + Tyr208Leu + Asn212Gln
 15 Pro195Asn + Gln200Asp + Thr202Gln + Tyr203Gln + Pro204Ser
 + Ser206Glu + Thr207Pro + Asn212Ser + Gly213Gln
 Ala194Gln + Pro195Gln + Gly196Asn + Val199Ser + Gln200Asp
 + Thr202Ser + Gly205Ser + Ser206Glu + Ala209Ser
 Pro195Asn + Gly196Pro + Val197Cys + Val199Met + Gln200Asp
 20 + Ser206Glu + Thr207Ser + Ala209Gln + Leu211Val
 Pro195Gly + Val199Pro + Gln200Asp + Thr202Ser + Tyr203Gly
 + Pro204Gln + Ser206Asp + Leu211Met + Asn212Ser
 Gly196Pro + Val197Cys + Asn198Gln + Gln200Glu + Thr202Asn
 + Ser206Asp + Ala209Asn + Leu211Cys + Gly213Ser
 25 Pro195Gln + Asn198Ser + Gln200Glu + Thr202Asn + Pro204Gly
 + Ser206Asp + Thr207Ser + Tyr208Ser + Asn212Gln
 Gly196Asn + Asn198Ser + Val199Met + Gln200Asp + Thr202Ser
 + Tyr203His + Pro204Asn + Gly205Gln + Ser206Glu
 Ala194Thr + Asn198Gln + Val199Ala + Gln200Asp + Thr202Asn
 30 + Ser206Glu + Thr207Ser + Tyr208His + Gly213Gln
 Ala194Gln + Gly196Gln + Asn198Gln + Gln200Asp + Thr202Asn
 + Ser206Glu + Thr207Ser + Tyr208Thr + Gly213Gln

TABLE 32

	Loop 6 - Decuple Mutation Variants
35	Ala194Ser + Gly196Gln + Val197Ala + Asn198Gln + Thr202Pro + Pro204Ser + Gly205Ser + Thr207Pro + Leu211Val + Asn212Asp
40	Pro195Ser + Val197Gln + Val199His + Thr202Asn + Tyr203Pro + Gly205Gln + Ala209Thr + Ser210Glu + Asn212Ser + Thr214Gln
	Ala194Gly + Asn198Ser + Val199Ala + Thr202Gln + Tyr203Leu + Pro204Gly + Gly205Pro + Ala209His + Gly213Ser + Thr214Asp
45	Ala194His + Gly196Gln + Thr202Gly + Tyr203Val + Gly205Asn + Thr207Gln + Tyr208Cys + Ala209Ser + Gly213Gln + Thr214Asn
	Ala194Thr + Pro195Ser + Gly196Asn + Asn198Glu + Gln200Asn + Thr202Gly + Pro204Ser + Asn212Gln + Gly213Pro + Thr214Gly
50	Ala194Ser + Pro195Asn + Gly196Asn + Val199Thr + Thr202Gln + Pro204Asp + Thr207Asn + Tyr208Ser + Leu211Asn +

- Asn212Gln
 Pro195Asn + Gly196Ser + Val197Gly + Asn198Ser + Thr202Gly
 + Gly205Pro + Thr207Pro + Tyr208Asp + Ala209Ser +
 Thr214Asn
- 5 Ala194His + Pro195Gln + Gly196Asn + Asn198Gln + Val199His
 + Pro204Ser + Gly205Asn + Thr207Ser + Tyr208Ser +
 Thr214Ser
- Ala194Pro + Pro195Asn + Val197Asn + Val199Cys + Gln200Ser
 + Thr202Pro + Pro204Ser + Ser206Glu + Tyr208His +
- 10 Leu211Ile
- Ala194Thr + Val197Met + Asn198Asp + Val199Gly + Gln200Ser
 + Tyr203Gln + Pro204Asn + Thr207Gln + Ala209Pro +
 Leu211Ala
- Ala194Pro + Pro195Gly + Val197Asn + Asn198Ser + Val199His
 + Tyr208His + Ala209Asp + Leu211Thr + Asn212Gln +
- 15 Thr214Gln
- Pro195Ser + Val199Met + Thr202Ser + Tyr203Ile + Gly205Gln
 + Ser206Asp + Tyr208His + Leu211Pro + Asn212Gln +
 Gly213Pro
- 20 Ala194Thr + Val197Ser + Val199Asn + Thr202Gln + Tyr203Met
 + Gly205Pro + Ser206Glu + Tyr208Ile + Ala209Asn +
 Gly213Ser
- Ala194Thr + Val197Gln + Asn198Gln + Val199Gly + Thr202Ser
 + Pro204Ser + Gly205Pro + Thr207Asn + Ala209Pro +
- 25 Thr214Asn
- Ala194His + Pro195Asn + Gly196Asn + Val199Thr + Gln200Asn
 + Thr202Asn + Tyr203Ala + Gly208Asp + Thr207Gly +
 Thr214Pro
- Ala194Ser + Pro195Gly + Gly196Ser + Val197Pro + Asn198Gln
 + Val199Thr + Thr202Pro + Tyr203Met + Pro204Gln +
- 30 Gly205Gln
- Ala194Thr + Pro195Gln + Val197Asp + Gln200Ser + Thr202Pro
 + Pro204Ser + Gly205Gln + Thr207Gly + Tyr208His +
 Ala209Gly
- 35 Ala194Pro + Pro195Ser + Asn198Ser + Val199Gln + Gln200Asp
 + Thr202Gln + Tyr203Asn + Pro204Gly + Leu211Val +
 Thr214Pro
- Pro195Ser + Gly196Gln + Val199Pro + Gln200Asn + Tyr203Gln
 + Thr207Asp + Ala209His + Leu211His + Asn212Gln +
- 40 Thr214Gly
- Gly196Pro + Asn198Ser + Val199Gly + Gln200Ser + Thr202Asn
 + Tyr203Ser + Tyr208Leu + Ala209His + Leu211Asp +
 Asn212Asp
- Gly196Asn + Val199Ala + Gln200Ser + Thr202Gln + Tyr203His
 + Pro204Asn + Gly205Pro + Asn212Gln + Gly213Glu +
- 45 Thr214Glu
- Gly196Pro + Val199Ser + Gln200Ser + Thr202Pro + Pro204Gln
 + Ala209Glu + Ser210Glu + Asn212Ser + Gly213Ser +
 Thr214Ser
- 50 Val197Thr + Asn198Gln + Val199Gln + Pro204Gly + Thr207Pro
 + Ala209Asp + Ser210Glu + Asn212Ser + Gly213Ser +
 Thr214Ser
- Ala194Pro + Pro195Gln + Val197Ala + Val199Gln + Gln200Ser
 + Pro204Gln + Gly205Pro + Tyr208Met + Ala209Asp +

Ser210Glu
 Pro195Gly + Val197Gly + Asn198Gln + Thr202Gly + Tyr203Ala
 + Gly205Pro + Ala209Glu + Ser210Glu + Leu211Ser +
 Gly213Gln
 5 Pro195Ser + Gly196Asn + Asn198Gln + Gln200Ser + Thr202Gly
 + Pro204Gln + Tyr208Thr + Leu211Cys + Asn212Glu +
 Gly213Glu
 Gly196Gln + Val197Ser + Gln200Ser + Thr202Pro + Pro204Asp
 + Gly205Asp + Tyr208Gln + Ala209Pro + Asn212Ser +
 10 Thr214Gln
 Ala194Pro + Pro195Gln + Gly196Gln + Pro204Asp + Gly205Glu
 + Tyr208Ala + Ala209Ser + Leu211Asn + Gly213Asn +
 Thr214Ser
 Ala194Thr + Val197Cys + Val199Met + Gln200Ser + Gly205Pro
 15 + Tyr208Thr + Ser210Glu + Leu211Asp + Asn212Ser +
 Gly213Pro
 Ala194Gly + Val197His + Thr202Ser + Tyr203Asn + Thr207Pro
 + Tyr208Cys + Ser210Glu + Leu211Glu + Asn212Gln +
 Gly213Pro
 20 Val197His + Asn198Ser + Gln200Ser + Thr202Asn + Gly205Ser
 + Tyr208Gln + Ser210Glu + Leu211Glu + Asn212Ser +
 Thr214Pro
 Ala194Thr + Gly196Asn + Asn198Gln + Gln200Asn + Thr202Pro
 + Tyr203Thr + Gly205Asn + Ser210Glu + Leu211Glu +
 25 Asn212Ser
 Ala194Gly + Gly196Gln + Asn198Ser + Val199Cys + Pro204Asn
 + Gly205Asp + Ser206Asp + Thr207Gln + Ala209Gly +
 Gly213Asn
 Pro195Gln + Val197Met + Val199Ala + Gln200Ser + Gly205Asp
 30 + Ser206Asp + Thr207Asn + Tyr208Gln + Leu211Pro +
 Asn212Ser
 Ala194His + Pro195Gln + Asn198Gln + Thr202Pro + Gly205Glu
 + Ser206Asp + Thr207Pro + Leu211Thr + Gly213Ser +
 Thr214Gln
 35 Gly196Pro + Asn198Gln + Val199Gly + Gln200Ser + Thr202Asn
 + Pro204Asn + Gly205Glu + Ser206Asp + Thr207Gly +
 Thr214Gln
 Pro195Gln + Val197His + Asn198Gln + Thr202Gly + Gly205Asp
 + Ser206Glu + Thr207Ser + Tyr208Ala + Asn212Gln +
 40 Gly213Asn
 Ala194Asn + Gly196Asn + Val197Ser + Asn198Ser + Val199Met
 + Thr202Asn + Tyr203Ala + Gly205Asp + Ser206Asp +
 Thr214Asn
 Ala194Thr + Pro195Asn + Gly196Gln + Val199Thr + Gln200Asn
 45 + Thr202Ser + Pro204Asn + Gly205Asp + Ser206Glu +
 Thr207Asn
 Pro195Ser + Gly196Ser + Val197Pro + Asn198Gln + Gln200Asn
 + Tyr203Leu + Gly205Asp + Ser206Glu + Asn212Ser +
 Thr214Pro
 50 Pro195Ser + Gly196Pro + Val197Ser + Gln200Ser + Thr202Pro
 + Tyr203Val + Pro204Gly + Gly205Glu + Ser206Glu +
 Tyr208Met
 Ala194Gly + Gly196Gln + Gln200Ser + Thr202Ser + Pro204Asn
 + Ser206Asp + Thr207Asp + Ala209Gln + Leu211Met +

Thr214Pro
 Gly196Asn + Val197Ser + Val199Ala + Tyr203Ile + Ser206Asp
 + Thr207Glu + Ala209Ser + Leu211Ala + Asn212Ser +
 Thr214Asn
 5 Ala194Ser + Pro204Asn + Gly205Ser + Ser206Asp + Thr207Glu
 + Tyr208Met + Ala209Asn + Leu211Ile + Asn212Gln +
 Gly213Asn
 Ala194Gln + Asn198Gln + Val199Asn + Thr202Gln + Tyr203Ile
 + Gly205Gln + Ser206Asp + Thr207Glu + Tyr208Ser +
 10 Gly213Ser
 Gly196Gln + Asn198Gln + Thr202Gln + Pro204Ser + Gly205Ser
 + Ser206Glu + Thr207Asp + Leu211Ile + Gly213Pro +
 Thr214Pro
 Pro195Asn + Gly196Gln + Val197Gln + Thr202Asn + Gly205Ser
 15 + Ser206Glu + Thr207Glu + Tyr208Ile + Gly213Gln +
 Thr214Asn
 Asn198Ser + Thr202Ser + Tyr203Ile + Gly205Asn + Thr207Asn
 + Tyr208Asp + Ala209Glu + Leu211Ile + Gly213Ser +
 Thr214Ser
 20 Val199His + Gln200Glu + Tyr203Met + Pro204Gly + Thr207Pro
 + Ala209Thr + Ser210Glu + Leu211Asn + Asn212Ser +
 Gly213Pro
 Ala194His + Gly196Ser + Asn198Ser + Gln200Glu + Thr202Gln
 + Tyr203Gln + Gly205Pro + Thr207Gly + Ser210Glu +
 25 Gly213Asn
 Gly196Pro + Val199Asn + Gln200Glu + Pro204Gly + Tyr208His
 + Ser210Asp + Leu211Gln + Asn212Ser + Gly213Gln +
 Thr214Asn
 Pro195Gly + Gly196Pro + Gln200Asp + Tyr203Asn + Pro204Asn
 30 + Gly205Asn + Thr207Asn + Tyr208Ile + Ser210Asp +
 Gly213Gln
 Ala194Gln + Pro195Gln + Gly196Gln + Val197Gln + Gln200Asp
 + Thr207Gly + Ala209Asn + Ser210Asp + Leu211Gly +
 Gly213Asn
 35 Val197Thr + Val199Ser + Gln200Glu + Tyr203Asn + Pro204Gly
 + Thr207Asn + Tyr208Gly + Ser210Glu + Asn212Ser +
 Thr214Asn
 Gly196Gln + Val197Gln + Val199Asn + Gln200Glu + Tyr203Asn
 + Thr207Gln + Ala209Gly + Ser210Glu + Asn212Gln +
 40 Gly213Gln
 Pro195Asn + Val197Met + Val199Cys + Gln200Asp + Thr202Asn
 + Thr207Ser + Tyr208Gly + Ala209Gln + Ser210Glu +
 Leu211Asn
 Ala194Asn + Val199Gln + Gln200Asp + Tyr203Gly + Pro204Ser
 45 + Gly205Pro + Tyr208Ile + Ser210Glu + Leu211Asn +
 Gly213Ser
 Ala194His + Pro195Gln + Val197Glu + Asn198Ser + Val199Ser
 + Tyr203His + Thr207Pro + Leu211Gln + Asn212Glu +
 Gly213Ser
 50 Gly196Ser + Val197Glu + Asn198Gln + Val199Cys + Tyr203Pro
 + Pro204Gly + Ala209Gln + Asn212Glu + Gly213Gln +
 Thr214Asn
 Gly196Ser + Val197Gly + Asn198Asp + Gln200Ser + Tyr203Pro
 + Tyr208Ala + Ala209Gly + Ser210Glu + Leu211Ile +

Thr214Asn
 Gly196Pro + Asn198Asp + Val199Gln + Gln200Asn + Pro204Gln
 + Gly205Pro + Thr207Gly + Ser210Asp + Asn212Gln +
 Gly213Ser
 5 Pro195Asn + Gly196Ser + Val197Gln + Asn198Glu + Gln200Ser
 + Pro204Gly + Tyr208Gln + Ala209Asn + Ser210Glu +
 Gly213Pro
 Asn198Asp + Val199Met + Gln200Asn + Thr202Gln + Pro204Asn
 + Gly205Gln + Tyr208Ala + Ala209His + Ser210Glu +
 10 Thr214Pro
 Ala194Gln + Val197Ala + Asn198Glu + Gln200Asn + Thr202Gly
 + Pro204Gln + Gly205Gln + Tyr208Thr + Ser210Asp +
 Leu211Val
 Val197Ser + Asn198Asp + Val199Asn + Gln200Ser + Pro204Ser
 15 + Thr207Pro + Tyr208Leu + Ser210Glu + Asn212Gln +
 Thr214Ser
 Ala194Thr + Gly196Asn + Val197Ser + Asn198Glu + Val199Asn
 + Gln200Ser + Thr202Ser + Thr207Ser + Ser210Glu +
 Gly213Ser
 20 Gly196Pro + Val197Met + Asn198Asp + Val199Gly + Gln200Asn
 + Tyr203Pro + Gly205Asn + Tyr208Val + Ser210Asp +
 Leu211His
 Gly196Gln + Asn198Asp + Gln200Asn + Tyr203Asn + Gly205Pro
 + Thr207Ser + Tyr208Gln + Ala209Pro + Leu211Glu +
 25 Asn212Gln
 Pro195Asn + Val197Pro + Asn198Glu + Val199Cys + Tyr203Asn
 + Thr207Gly + Tyr208Gln + Ala209Ser + Leu211Glu +
 Gly213Asn
 Ala194Gln + Gly196Gln + Val199Met + Gln200Asp + Tyr203Cys
 30 + Thr207Ser + Ala209Asp + Asn212Ser + Gly213Gln +
 Thr214Gln
 Pro195Asn + Gly196Pro + Asn198Ser + Gln200Glu + Thr202Ser
 + Thr207Gln + Tyr208Ala + Ala209Glu + Leu211Ala +
 Asn212Gln
 35 Pro195Gly + Gly196Asn + Val199Gln + Thr202Gly + Pro204Glu
 + Gly205Gln + Ser206Glu + Thr207Ser + Leu211Gln +
 Asn212Gln
 Pro195Gly + Gln200Asn + Tyr203Leu + Pro204Glu + Ser206Asp
 + Tyr208Gln + Ala209Gln + Asn212Gln + Gly213Pro +
 40 Thr214Gln
 Ala194His + Pro195Ser + Val199Thr + Thr202Gly + Tyr203Cys
 + Pro204Glu + Ser206Glu + Leu211His + Asn212Ser +
 Gly213Pro
 Pro195Gln + Val197Gln + Asn198Gln + Gln200Ser + Pro204Glu
 45 + Gly205Ser + Ser206Asp + Ala209Gly + Asn212Ser +
 Thr214Gln
 Ala194Thr + Asn198Asp + Val199Ala + Gln200Asn + Gly205Pro
 + Tyr208Ser + Ala209Gly + Leu211Val + Asn212Glu +
 Gly213Gln
 50 Ala194Gly + Pro195Gln + Val199Cys + Tyr203Leu + Pro204Ser
 + Gly205Glu + Thr207Asp + Ala209Gln + Asn212Gln +
 Thr214Gly
 Pro195Gln + Val197Gln + Gln200Ser + Thr202Gln + Pro204Glu
 + Gly205Ser + Thr207Asp + Leu211His + Asn212Ser +

Thr214Ser
 Ala194Asn + Pro195Ser + Val197Ser + Asn198Gln + Thr202Asn
 + Pro204Asp + Thr207Glu + Leu211His + Asn212Ser +
 Gly213Ser
 5 Ala194Thr + Pro195Ser + Val197Gln + Asn198Glu + Val199Met
 + Gln200Asp + Pro204Gly + Gly205Ser + Ala209Asn +
 Thr214Asn
 Pro195Gln + Gly196Pro + Val197Met + Asn198Asp + Val199Ala
 + Gln200Glu + Thr202Pro + Tyr203Ile + Tyr208Cys +
 10 Leu211Thr
 Ala194Gln + Gly196Asn + Asn198Glu + Val199Ala + Gln200Asp
 + Thr202Ser + Tyr203Cys + Thr207Asn + Tyr208Met +
 Gly213Asn
 Ala194Thr + Val197Pro + Val199His + Gln200Asp + Thr202Gln
 + Tyr203Met + Gly205Ser + Thr207Asn + Tyr208Asp +
 15 Asn212Ser
 Pro195Asn + Val197Asp + Asn198Gln + Val199Gly + Gln200Ser
 + Thr207Ser + Tyr208Ile + Ala209Asn + Asn212Ser +
 Gly213Asp
 20 Pro195Asn + Val197Pro + Asn198Gln + Gln200Glu + Gly205Gln
 + Tyr208Gly + Ala209Gly + Leu211Glu + Asn212Ser +
 Thr214Ser
 Ala194Thr + Gly196Ser + Asn198Ser + Gln200Asp + Thr202Gly
 + Tyr203Met + Gly205Gln + Tyr208Ala + Leu211Asp +
 25 Thr214Asn
 Pro195Ser + Asn198Ser + Val199Thr + Thr202Asn + Gly205Asn
 + Thr207Ser + Ala209Gly + Leu211Glu + Asn212Gln +
 Gly213Asp
 Pro195Gln + Gly196Gln + Asn198Ser + Thr202Pro + Pro204Asn
 + Thr207Asp + Tyr208Gly + Ala209Asp + Leu211Ile +
 30 Asn212Ser
 Ala194Gly + Pro195Gly + Asn198Ser + Gln200Asn + Thr202Asn
 + Tyr203Ala + Tyr208Val + Ser210Glu + Asn212Asp +
 Thr214Gly
 35 Ala194Gln + Pro195Gln + Asn198Gln + Gln200Asn + Thr202Gly
 + Tyr203Leu + Gly205Gln + Ala209Gln + Ser210Glu +
 Asn212Glu
 Pro195Gln + Val197Gly + Val199Gly + Thr202Asn + Gly205Pro
 + Thr207Asn + Ala209Asn + Ser210Glu + Leu211Met +
 40 Asn212Glu
 Ala194Thr + Pro195Gly + Gly196Pro + Asn198Ser + Thr207Pro
 + Tyr208Cys + Ala209Ser + Ser210Glu + Leu211Ser +
 Asn212Asp
 Ala194His + Pro195Ser + Gly196Gln + Val197Ala + Val199Asn
 + Tyr203Gln + Thr207Asn + Tyr208His + Ser210Asp +
 45 Asn212Glu
 Ala194Gln + Pro195Asn + Gly196Ser + Val197Met + Pro204Ser
 + Gly205Pro + Thr207Ser + Tyr208Ala + Ser210Glu +
 Asn212Glu
 50 Ala194Ser + Val199Thr + Thr202Ser + Tyr203Ala + Pro204Asn
 + Gly205Pro + Ser210Asp + Leu211Ala + Asn212Asp +
 Thr214Pro
 Pro195Asn + Thr202Gln + Pro204Ser + Thr207Gly + Tyr208Glu
 + Ala209Asn + Ser210Glu + Leu211Asn + Asn212Gln +

Gly213Asn
 Gly196Asn + Val197Thr + Val199Thr + Pro204Ser + Thr207Gln
 + Tyr208Asp + Ser210Asp + Leu211Thr + Asn212Gln +
 Thr214Asn
 5 Alal94Asn + Pro195Asn + Val199Cys + Gln200Asn + Pro204Gln
 + Thr207Ser + Tyr208Glu + Ser210Asp + Leu211Asn +
 Asn212Gln
 Alal94Thr + Gly196Pro + Val199His + Gln200Ser + Gly205Asn
 + Ser206Glu + Tyr208Glu + Ala209Thr + Leu211Met +
 10 Thr214Ser
 Alal94Ser + Pro195Gln + Asn198Gln + Val199His + Pro204Asn
 + Gly205Gln + Ser206Glu + Tyr208Asp + Ala209Thr +
 Gly213Asn
 Gly196Gln + Val197Met + Val199Ser + Gln200Ser + Thr202Asn
 15 + Pro204Asn + Tyr208Thr + Ala209Gln + Asn212Glu +
 Thr214Asp
 Val197Ala + Asn198Ser + Gln200Ser + Thr202Gly + Pro204Gln
 + Thr207Gln + Tyr208Gln + Ala209His + Asn212Glu +
 Thr214Asp
 20 Alal94Pro + Gly196Ser + Val197Asp + Val199Asn + Thr202Asn
 + Tyr203Val + Thr207Gln + Ala209Asn + Ser210Glu +
 Asn212Gln
 Pro195Ser + Val197Glu + Asn198Gln + Val199Gln + Tyr203Leu
 + Tyr208Val + Ala209Asn + Asn212Gln + Gly213Pro +
 25 Thr214Glu
 Pro195Gln + Gly196Pro + Val197Asn + Asn198Glu + Gln200Ser
 + Pro204Asn + Gly205Asn + Leu211Cys + Asn212Gln +
 Gly213Asp
 Pro195Gln + Gly196Pro + Val197Thr + Asn198Asp + Thr202Pro
 30 + Tyr203Gln + Thr207Gly + Ala209Glu + Gly213Ser +
 Thr214Ser
 Alal94Ser + Pro195Gln + Val197Pro + Asn198Asp + Val199Ala
 + Tyr203Thr + Pro204Gln + Ala209Asp + Leu211Val +
 Asn212Ser
 35 Pro195Gly + Val197Glu + Asn198Gln + Gln200Asp + Tyr203His
 + Pro204Ser + Thr207Gly + Tyr208His + Gly213Pro +
 Thr214Gly
 Pro195Gly + Gly196Pro + Val199Thr + Gln200Glu + Tyr203Met
 + Pro204Gln + Gly205Pro + Tyr208Ser + Asn212Asp +
 40 Gly213Pro
 Gly196Pro + Val197Ser + Val199Pro + Gln200Glu + Thr207Gly
 + Ala209Gly + Leu211Gln + Asn212Asp + Gly213Pro +
 Thr214Asn
 Alal94His + Pro195Gln + Gly196Asn + Val197Ser + Gln200Glu
 45 + Tyr203Ala + Pro204Asn + Gly205Ser + Thr207Pro +
 Asn212Glu
 Alal94Ser + Pro195Asn + Gly196Pro + Asn198Ser + Val199Thr
 + Tyr208Ile + Leu211Glu + Asn212Gln + Gly213Ser +
 Thr214Glu
 50 Alal94Pro + Pro195Asn + Asn198Ser + Val199Met + Tyr203Met
 + Gly205Pro + Thr207Pro + Tyr208Ser + Leu211Glu +
 Thr214Glu
 Alal94His + Pro195Gln + Gly196Gln + Val199Pro + Tyr203His
 + Thr207Asn + Ala209Asp + Leu211Ala + Asn212Glu +

Thr214Asn
 Ala194His + Gly196Gln + Thr202Ser + Tyr203Gly + Pro204Gly
 + Gly205Ser + Ser206Asp + Thr207Gln + Ala209Asp +
 Thr214Pro
 5 Pro195Gln + Thr202Ser + Pro204Gln + Gly205Pro + Ser206Asp
 + Tyr208Met + Ala209Glu + Asn212Gln + Gly213Pro +
 Thr214Ser
 Gly196Gln + Val197Pro + Thr202Asn + Tyr203Gly + Gly205Pro
 + Ser206Glu + Thr207Ser + Ala209Glu + Leu211Gln +
 10 Asn212Ser
 Ala194Asn + Pro195Ser + Gly196Pro + Val199Ala + Thr202Gln
 + Pro204Gln + Ser206Asp + Ala209Glu + Leu211His +
 Asn212Ser
 Gly196Ser + Asn198Ser + Val199Ser + Gln200Asn + Tyr203Asn
 15 + Gly205Gln + Ser206Glu + Ala209Glu + Leu211Ser +
 Gly213Gln
 Ala194Thr + Val197Cys + Val199Asn + Pro204Gly + Ser206Asp
 + Thr207Gly + Tyr208Gly + Ala209Glu + Leu211Ile +
 Thr214Gln
 20 Ala194Gly + Pro195Ser + Gln200Ser + Thr202Gly + Tyr203Leu
 + Pro204Gly + Gly205Pro + Ser206Asp + Ala209Asp +
 Thr214Gly
 Pro195Ser + Gly196Pro + Val199His + Gln200Asp + Thr202Pro
 + Gly205Pro + Thr207Asp + Ala209Thr + Asn212Gln +
 25 Gly213Gln
 Ala194Gln + Gly196Asn + Asn198Gln + Val199Pro + Gln200Asp
 + Thr202Gly + Tyr203Thr + Gly205Pro + Thr207Asp +
 Ala209Gln
 Pro195Asn + Val197Thr + Val199Ala + Gln200Asn + Tyr203Asn
 30 + Gly205Pro + Thr207Gly + Ser210Asp + Asn212Gln +
 Gly213Glu
 Ala194Asn + Pro195Gln + Val197Asn + Val199Asn + Pro204Gly
 + Thr207Pro + Ser210Asp + Asn212Ser + Gly213Glu +
 Thr214Pro
 35 Ala194Gln + Pro195Asn + Val197Gly + Tyr203Met + Pro204Ser
 + Tyr208Gln + Ala209Asn + Ser210Glu + Asn212Ser +
 Gly213Glu
 Ala194His + Gly196Ser + Tyr203Asn + Pro204Gly + Gly205Pro
 + Ala209Ser + Ser210Glu + Leu211Pro + Asn212Ser +
 40 Gly213Asp
 Gly196Pro + Gln200Asn + Thr202Asn + Tyr203His + Gly205Asp
 + Tyr208Ile + Ala209Glu + Leu211Met + Gly213Pro +
 Thr214Pro
 Val197His + Val199Asn + Gln200Asn + Thr202Ser + Tyr203Ser
 45 + Gly205Glu + Tyr208Ser + Ala209Asp + Gly213Pro +
 Thr214Pro
 Ala194Asn + Val197Pro + Gln200Ser + Thr202Gln + Tyr203Met
 + Gly205Gln + Thr207Asp + Ser210Asp + Leu211Ser +
 Asn212Ser
 50 Ala194Thr + Asn198Ser + Tyr203Asn + Gly205Pro + Thr207Asp
 + Ala209Gln + Ser210Glu + Leu211Val + Asn212Ser +
 Thr214Ser
 Asn198Gln + Val199Pro + Gln200Asn + Thr202Gln + Tyr203Asn
 + Thr207Asp + Ala209Pro + Ser210Glu + Asn212Ser +

Gly213Asn
Ala194Ser + Pro195Asn + Asn198Gln + Val199Ala + Gln200Asp
+ Tyr203His + Ala209Thr + Leu211Ser + Gly213Asp +
Thr214Ser
5 Ala194Pro + Pro195Asn + Gly196Pro + Val197Ser + Gln200Asp
+ Tyr208Cys + Leu211Gln + Asn212Ser + Gly213Asp +
Thr214Gly
Ala194Gln + Pro195Ser + Gly196Gln + Asn198Asp + Gln200Ser
+ Thr202Ser + Tyr208Asp + Ala209Thr + Leu211His +
10 Thr214Asn
Ala194Asn + Pro195Gln + Val197Thr + Asn198Asp + Pro204Asn
+ Thr207Ser + Tyr208Asp + Leu211Ile + Gly213Gln +
Thr214Gln
Ala194Gln + Pro195Asn + Val199Asn + Tyr203Ser + Pro204Asp
15 + Thr207Asn + Ser210Asp + Leu211Gly + Asn212Ser +
Gly213Ser
Ala194Asn + Pro195Asn + Thr202Gly + Pro204Asp + Tyr208Ile
+ Ala209Gly + Ser210Asp + Leu211Val + Asn212Gln +
Thr214Ser
20 Ala194Asn + Gly196Ser + Asn198Ser + Val199Pro + Tyr203His
+ Pro204Glu + Gly205Gln + Tyr208Met + Ala209Thr +
Ser210Glu
Ala194Thr + Asn198Ser + Val199Thr + Thr202Asn + Pro204Glu
+ Gly205Asn + Thr207Gln + Ala209His + Ser210Glu +
25 Thr214Gly
Ala194His + Pro195Gln + Asn198Ser + Val199Gly + Tyr203Gln
+ Pro204Asp + Thr207Gly + Ser210Glu + Asn212Gln +
Gly213Ser
Pro195Asn + Tyr203Ser + Pro204Glu + Gly205Pro + Tyr208His
30 + Ala209Gly + Ser210Glu + Leu211Pro + Gly213Pro +
Thr214Asn
Gly196Asn + Asn198Ser + Gln200Ser + Thr202Gly + Pro204Asp
+ Gly205Asn + Ala209Thr + Ser210Glu + Gly213Pro +
Thr214Ser
35 Gln200Ser + Thr202Gln + Tyr203Met + Pro204Asp + Gly205Pro
+ Tyr208Cys + Ala209Gly + Ser210Asp + Leu211Thr +
Gly213Gln
Ala194Pro + Gly196Asn + Gln200Ser + Tyr203Ser + Pro204Glu
+ Thr207Gly + Ala209Asn + Ser210Asp + Leu211Val +
40 Thr214Ser
Val199His + Gln200Ser + Thr202Ser + Pro204Asp + Gly205Asn
+ Tyr208Pro + Ser210Asp + Leu211Pro + Gly213Pro +
Thr214Pro
Ala194Ser + Pro195Asn + Gly196Ser + Val197Ser + Asn198Gln
45 + Val199Ser + Pro204Glu + Tyr208Leu + Ser210Asp +
Leu211Ser
Ala194His + Gly196Pro + Val199Gly + Gln200Asp + Pro204Glu
+ Tyr208Gln + Ala209Gly + Leu211Ser + Asn212Ser +
Thr214Asn
50 Ala194Gln + Val197Pro + Val199Asn + Gln200Asp + Thr202Gln
+ Pro204Asp + Gly205Asn + Tyr208His + Ala209Asn +
Leu211Ile
Pro195Ser + Val197Met + Asn198Ser + Gln200Asp + Thr202Gly
+ Tyr203Gln + Pro204Glu + Thr207Pro + Asn212Ser +

Thr214Gly
 Pro195Ser + Val199Met + Gln200Ser + Pro204Gln + Thr207Ser
 + Ala209Glu + Leu211Ala + Asn212Gln + Gly213Glu +
 Thr214Gly
 5 Pro195Gln + Gly196Pro + Asn198Ser + Val199Gly + Tyr203Asn
 + Gly205Asn + Thr207Pro + Ala209Glu + Leu211Val +
 Gly213Asp
 Ala194Asn + Pro195Gln + Asn198Ser + Val199Ser + Gly205Asn
 + Thr207Glu + Ala209Ser + Leu211Glu + Asn212Gln +
 10 Thr214Ser
 Ala194Ser + Asn198Ser + Gln200Ser + Thr202Gly + Tyr203Leu
 + Thr207Gly + Ala209His + Ser210Glu + Asn212Ser +
 Thr214Asp
 Gly196Ser + Gln200Asn + Thr202Pro + Tyr203Leu + Pro204Asn
 15 + Thr207Gln + Ser210Asp + Leu211Ala + Gly213Pro +
 Thr214Asp
 Gly196Ser + Asn198Gln + Tyr203Gly + Pro204Gln + Gly205Pro
 + Thr207Pro + Tyr208His + Ser210Glu + Gly213Gln +
 Thr214Asp
 20 Val197Thr + Val199Thr + Gln200Ser + Thr202Ser + Gly205Asn
 + Thr207Pro + Tyr208Cys + Ser210Glu + Gly213Ser +
 Thr214Asp
 Gly196Gln + Val197Thr + Gln200Asp + Thr202Asn + Tyr203His
 + Ser206Glu + Thr207Ser + Tyr208Pro + Leu211Pro +
 25 Asn212Gln
 Val197Met + Val199Gln + Gln200Glu + Thr202Gln + Pro204Gln
 + Gly205Asn + Ser206Asp + Thr207Gln + Leu211Val +
 Thr214Ser
 Ala194Thr + Pro195Gly + Gly196Asn + Val197Ser + Gln200Glu
 30 + Thr202Pro + Gly205Pro + Ser206Glu + Leu211Met +
 Asn212Ser
 Pro195Ser + Gly196Gln + Val199Cys + Gln200Glu + Ser206Glu
 + Tyr208Thr + Leu211Gln + Asn212Gln + Gly213Pro +
 Thr214Asn
 35 Gly196Gln + Val197Gly + Asn198Gln + Gln200Glu + Gly205Asn
 + Ser206Glu + Thr207Pro + Ala209Asn + Asn212Gln +
 Gly213Ser
 Pro195Gln + Val197Gly + Gln200Glu + Thr202Gln + Tyr203Val
 + Gly205Gln + Ser206Asp + Tyr208Met + Ala209Pro +
 40 Thr214Gly
 Ala194Ser + Pro195Asn + Val197Thr + Val199Thr + Gln200Glu
 + Thr202Pro + Tyr203Ser + Gly205Pro + Ser206Glu +
 Thr214Gly
 Pro195Ser + Gln200Glu + Thr202Gln + Tyr203Gly + Gly205Pro
 45 + Ser206Asp + Thr207Gly + Ala209His + Leu211His +
 Thr214Gly
 Ala194Asn + Pro195Gly + Gly196Asn + Val197Cys + Val199Asn
 + Gln200Glu + Tyr203Pro + Pro204Gln + Ser206Asp +
 Leu211Ala
 50 Ala194Thr + Pro195Asn + Gly196Gln + Val197Asn + Gln200Glu
 + Thr202Ser + Ser206Glu + Ala209His + Leu211Ala +
 Thr214Ser
 Val199Gly + Gln200Glu + Thr202Gln + Pro204Asn + Gly205Pro
 + Ser206Asp + Thr207Ser + Ala209Gly + Leu211Cys +

Asn212Ser
 Ala194Thr + Val197Ser + Val199Gln + Gln200Asp + Thr202Gln
 + Pro204Gln + Ser206Glu + Ala209Gly + Leu211His +
 Gly213Gln
 5 Ala194Gly + Gly196Asn + Asn198Gln + Gln200Glu + Gly205Pro
 + Ser206Asp + Ala209His + Leu211Pro + Gly213Gln +
 Thr214Gly
 Gly196Ser + Val199Ser + Thr202Ser + Pro204Asp + Thr207Asn
 + Tyr208Leu + Leu211Glu + Asn212Gln + Gly213Ser +
 10 Thr214Pro
 Ala194Pro + Pro195Asn + Val197Pro + Thr202Pro + Tyr203Thr
 + Thr207Gln + Tyr208Glu + Asn212Glu + Gly213Ser +
 Thr214Ser
 Gly196Asn + Gln200Ser + Gly205Pro + Thr207Gln + Tyr208Asp
 + Ala209Ser + Leu211Ser + Asn212Glu + Gly213Pro +
 15 Thr214Pro
 Ala194Gly + Val199Pro + Gln200Asp + Thr202Pro + Tyr203Cys
 + Pro204Gly + Ala209Gln + Leu211Cys + Asn212Gln +
 Thr214Asp
 20 Gly196Ser + Val197Gly + Gln200Asp + Tyr203Cys + Pro204Ser
 + Thr207Gln + Leu211Ala + Asn212Gln + Gly213Ser +
 Thr214Asp
 Ala194Pro + Val197Thr + Thr202Gln + Tyr203Met + Pro204Asn
 + Ser206Asp + Tyr208His + Ala209His + Ser210Asp +
 25 Thr214Asn
 Gly196Asn + Val197Cys + Thr202Asn + Tyr203Met + Gly205Pro
 + Ser206Asp + Thr207Gly + Ala209Pro + Ser210Asp +
 Gly213Gln
 Ala194Thr + Val197Ser + Val199His + Thr202Gln + Tyr203Ser
 + Ser206Asp + Thr207Ser + Ser210Asp + Gly213Pro +
 30 Thr214Pro
 Ala194Thr + Pro195Ser + Gly196Asn + Val197Pro + Asn198Gln
 + Thr202Gln + Ser206Glu + Ser210Glu + Asn212Ser +
 Thr214Gly
 35 Pro195Asn + Gly196Ser + Val197Ser + Asn198Gln + Thr202Asn
 + Tyr203Met + Ser206Glu + Ser210Asp + Asn212Gln +
 Thr214Gln

TABLE 33

40	Multi-loop Double Mutation Variants
	Leu 94Gly + Gln200Glu
	Gln 57Ser + Asn 60Ser
	Val 93Gln + Gly213Asp
	Tyr102Cys + Thr207Gly
45	Ser154Glu + Asn198Gln
	Leu124Ile + Asn198Gln
	Ala209Gly + Ser210Glu
	Gln 57Asp + Leu 94Gly
	Leu 94Ala + Ser154Glu
50	Ser101Asp + Leu211Thr
	Ala131Glu + Gly196Gln
	Ser128Glu + Pro204Asn

	Ser103Asp + Pro129Asn
	Gly157Asn + Thr207Ser
	Gly 98Glu + Gly155Gln
	Gln200Asp + Ala209Pro
5	Asn 60Glu + Asn198Gln
	Leu 94Ile + Ser 99Asp
	Leu124Ile + Ser210Asp
	Ser126Glu + Thr202Ser
	Val 93Ala + Pro127Asp
10	Gly157Pro + Ser210Asp
	Val197Gly + Thr207Asp
	Gln185Glu + Ala194Thr
	Ser 97Glu + Tyr203Asn
	Gly100Pro + Thr207Asp
15	Ser210Asp + Leu211Met
	Tyr161Asn + Thr207Asp
	Leu124Ser + Pro127Asn
	Gly 61Ser + Thr207Pro
	Gly 98Glu + Gln200Ser
20	Gln200Asn + Asn212Glu
	Asp 58Glu + Ile105Cys
	Gly 61Pro + Ala209Thr
	Leu124Asp + Pro204Asn
	Gln 57Glu + Asn198Ser
25	Gln185Ser + Asn212Asp
	Phe183His + Val197Glu
	Asn 60Glu + Gln200Ser
	Gly 59Asn + Gly 61Glu
	Gly155Asp + Ile159Cys
30	Gly 63Gln + Leu211Gly
	Thr 64Pro + Tyr161Asp
	Leu 94Gln + Pro127Gly
	Thr207Gly + Gly213Glu
	Gln185Asp + Tyr203Ser
35	Gly 63Asn + Ala209Asn
	Tyr208Met + Gly213Asn
	Ser210Glu + Leu211Asn
	Tyr102Ala + Pro129Asn
	Gly125Glu + Leu211Gly
40	Ser103Asp + Thr207Ser
	Ser128Glu + Leu211His
	Gly155Gln + Leu211His
	Gln 57Asn + Gln200Asp
	Ser103Asp + Gly157Gln
45	Gly125Ser + Thr207Gly
	Ile105Pro + Val197Glu
	Pro204Asp + Ala209Gln
	Tyr161Asp + Thr207Asn
	Asn198Ser + Ser210Asp
50	Gly 95Ser + Gln200Asp
	Gly 59Gln + Ala156Glu
	Gly 98Gln + Tyr102Cys
	Ala181His + Thr207Glu
	Ser154Glu + Pro204Ser